

Cancer Progress

a Bulletin of
Cancer Progress



**"interest rate
increased from
2 to 8 per cent"**

Such a notice from your bank would stimulate your immediate interest and action. Yet, opportunity for an equal four-fold investment increase, available for years, is being neglected. Eight instead of two out of ten patients with cancer of the uterine cervix could be saved by adequate public education concerning the importance of early diagnosis through periodic physical examinations and by appropriate use of existing therapeutic know-how.

First, although the value of early diagnosis of some types of cancer is disputed, there is no argument about its importance in cancer of the cervix.

Second, cancer of this site, like cancer of the larynx, usually expresses itself early in its course. (In spite of adequate warning, delay is the rule, and most women with this disease—more than four fifths of them—are first seen in moderately advanced conditions or worse.)

Third, examination is simple and diagnosis by smear and biopsy is an office procedure.

Fourth, evidence at hand suggests that cancer of the cervix may exist for varying periods of time in a noninvasive form—when it is 100 per cent curable. It appears to be possible to identify such intraepithelial cancer by means of the Papanicolaou smear—even though the cervix looks normal.

Finally, most gynecologists still subscribe to the principle of eliminating all erosions, lacerations, hyperplasias, infections, and inflammations as cancer prophylaxis.

These are persuasive arguments for investment—by patient and physician alike. The dividends can be expected to increase fourfold.

Cover—

The American Cancer Society's Award Medal presented to Dr. Ernest O. Lawrence, Director of the Radiation Laboratory, University of California. The Award, presented at the Society's Annual Dinner at the Hotel Roosevelt, New York City, on October 21, 1954, is in recognition of the Nobel Prize winner's work in developing the cyclotron, which led to the use of radioactive isotopes in the treatment of cancer.



NEWSLETTER

MARCH, 1955

NOTES FROM THE AMERICAN CANCER SOCIETY ANNUAL MEETING

(Continued from the January, 1955, Issue)

Pratt-Thomas and others (Medical College of South Carolina) reported inducing cervical cancer by applying human smegma to the cervical region of dba mice. This was accomplished by a minimum of seventy-eight injections over fourteen months. They theorized that bacterial action in the decomposing smegma might transform the cholesterol content into a carcinogenic agent.

Murphy (Bar Harbor, Maine) induced mouse cervical cancer by inserting a methylcholanthrene-coated thread or repeatedly painting the cervix with methylcholanthrene.

Hertz (N.C.I.) concluded from his observations of postmenopausal breast-cancer patients maintained on continuous massive doses of estrogen that endometrial cancer occasionally may be induced by estrogen. The response of premenopausal patients may be different, he said.

Mansell (Free Hospital for Women, Boston) found that many patients with endometrial carcinoma have as associated endocrine disturbances: diabetes (two or three times as much), obesity (in 25 to 30 per cent of the cases), and thyroid disease (in 3.1 per cent). She reported that granulosa-theca-cell ovarian tumors were associated with endometrial carcinoma and hyperplasia to some extent.

Detection and Diagnosis: Oppenheim and Rosenthal (N.Y.C. Dept. of Health) said that their one-cent, self-obtained cervical-smear method had proved practical. Women are given a simple kit -- 8-in. applicator tipped with collodion, slide and test tube of 95 per cent alcohol for fixing -- and told how to obtain a smear. When the procedure was explained personally, results were as good as when physicians took the smear (5 per cent unsatisfactory). When only written instructions were given in a relatively illiterate section of the city, 15 per cent of the slides proved unsatisfactory. Slides may be sent directly to a cytology laboratory or sent through a physician. Slides are classified as completely negative, atypical cells, suspicious, very sus-

picious, or positive. The investigators feel that if all women used this detection technique, cervical cancer would cease to be a major mortality factor. Cancers would be detected during their estimated average eight-year preinvasive and curable stage.

Erickson (U. of Tenn.) reported that 80,000 women in the Memphis area so far have been given routine vaginal smears over the last twenty-six months. Of the first 70,000 examined 1.9 per cent (1327) showed suspicious smears and were advised to have a biopsy. Of 1076 who had a biopsy, 544 were found to have cancer of the cervix or body of the uterus, 323 of them (60 per cent) unsuspected and unindicated in physicians' records. Another 129 had "borderline" atypicalities. A large percentage of the cancers were apparently early and presumably curable.

Hertig (Free Hospital for Women, Boston) reported that of 950 women given an artificial menopause by irradiation of the ovaries, nine developed endometrial cancers five to ten years later. He stated that women with benign cystic endometrial hyperplasia prior to the menopause are ten times more apt to develop endometrial carcinoma than women without this condition -- 1.5 per cent of the former developing cancer. When the hyperplasia is atypical (in contrast to the benign cystic types), however, a majority develop cancer. Tissue progresses from normal to malignant over a ten-year average period (minimum three years and maximum twenty-five years in this study). Carcinoma in situ tends to be present three to five years before the development of endometrial cancer, he said.

J. & R. Graham (Mass. Gen. Hosp.) are investigating the five per cent of cervical cases that are positive cytologically but in whom no cancers can be found. More than twenty such patients now are being followed. So far there are no answers to the questions: Was the cytological interpretation wrong? Did the lesions disappear spontaneously? Or are the cancers too well hidden for detection at this stage? Fennell (Pittsburgh) is also working on this project. The Grahams are continuing their prognostic studies based upon the response of normal epithelial cells to test radiation doses. Of patients giving a radiation-sensitive response, 69 per cent were five-year cures. Only 20 per cent of the radiation-resistant were five-year radiation cures. They recommend radiation for those with a sensitive response and surgery for the radiation resistant.

(Continued after page 72)



Keeping up

Some Early Contributions to Cancer Detection

Many of the histopathological procedures that are used in modern cancer diagnosis were first indicated by nineteenth century microscopists whose views were practically discarded only to be revived by our contemporaries. To facilitate sectioning of tissues, de Reimer (1760-1831) and Stilling (1810-1879) recommended freezing specimens; the technique holds its place today with improved methods of fixation that evolved later. Exfoliative cytology, although casually considered as a novel diagnostic practice, is a heritage from the eighth and possibly the sixth decade of the last century. Beale and other microscopists of almost a century ago highly recommended the examination of body ejecta for exfoliated cells and specified examination of urine, sputum, vomit, and discharges from the uterus and vagina. J. G. Richardson of Philadelphia, in 1871, quoted Beale and recommended exfoliative cytological methods in the diagnosis of cancer. The concept was developed further before 1885 by Carl Friedlaender who wrote, in *The Diagnosis of Carcinoma of the Uterus*: "In doubtful cases, however, where the question is whether we have to do with carcinoma or with a simple erosion, the examination of the secretion alone will never be sufficient; in such instances small bits are frequently excised, by the histological study of which the diagnosis should be confirmed." Aspiration as a method of obtaining biopsy material for the microscopic diagnosis of cancer was publicized by Francis Donaldson in 1853. The value

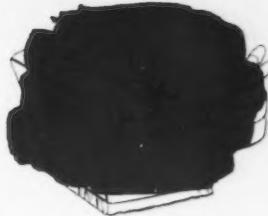
of frozen section; exfoliative-cytological study of serous effusions, excretions, and discharges; aspiration; and direct biopsy as diagnostic tools was known then; it is reaffirmed now.

Reimann, D. L.: Some nineteenth century contributions to cancer detection: an historical sketch. Obst. & Gynec. Surv. 9:495-500, Aug., 1954.

Chemotherapy of Leukemia

Since leukemia is a widespread systemic disease, the forms of treatment, such as surgery and obliterative radiation, that may be curative for localized cancers are not effective. Definite progress in the chemotherapy of leukemia has been made in the last ten years, and it would appear that this discipline offers the greatest promise for the future control of the disease. The probable avenues of approach in chemotherapy are the development of new agents with more prolonged therapeutic effect and applicability to a wider spectrum of leukemias, as well as the prevention of resistance to agents now in use. In acute leukemias, the therapeutic agents presently available include the antimetabolites amethopterin, aminopterin, and 6-mercaptopurine and the hormones ACTH and cortisone; the sequential use of these may be expected to produce beneficial effects with an increase in survival time in a high percentage of children. Definite but less frequent beneficial effects have been noted in adults with mercaptopurine. Irradiation either by local or total-body roentgen-ray or P³² therapy offers perhaps a wider range of applicability and technique than any of the chemotherapeutic agents in the treatment of the chronic

with Cancer



forms of leukemias. In chronic myelocytic leukemia, myleran, TEM, urethane, arsenic, and HN2 in order of preference are useful chemotherapeutic agents. In chronic lymphocytic leukemia, the only chemical agents of value are the mustard derivatives, TEM, HN2, the hormones, and possibly urethane.

Burchenal, J. H.: *The treatment of leukemia*. *Bull. New York Acad. Med.* 30:429-447, June, 1954.

Chemotherapy of Leukemia and Allied Diseases

The antimetabolite, 6-mercaptopurine, produced good hematological remissions in some children with acute leukemia. Daily oral administration of 2.5 mg. per Kg. rarely caused toxic manifestations in children, but continued dosage at this level in adults or at higher levels in children may produce bone-marrow depression or gastrointestinal symptoms. Of forty-five children with acute leukemia, fifteen had good remissions of two to twenty-two weeks after two to nine weeks on 6-MP. Partial remissions with an improvement in symptoms occurred in ten others. Four had hematological remissions that were complicated by steroid therapy or amethopterin. Two survived less than one week after 6-MP was begun, hence had an inadequate trial of the drug. Fourteen gave no response to 6-MP; thirteen of these were resistant to amethopterin and steroid therapy. Among those who responded, five had good clinical and hematological remissions and five had partial remissions among twenty-four resistant to amethopterin; some benefit was seen in eight of eighteen whose disease was re-

sistant to ACTH and cortisone. In a total of thirty-five patients (children as well as adults) with lymphomas and miscellaneous carcinomas and sarcoma, 6-MP did not produce any definite clinical improvement at doses that produce hematological toxicity.

There is evidence that therapeutic resistance of the acute leukemias to 6-MP develops somewhat more rapidly than it does to the folic acid antagonists but there is no evidence, as yet, that there is cross resistance between these two. Since the mode of action of 6-MP appears to differ from that of other agents hitherto employed clinically in the treatment of leukemia, the compound appears to be of practical interest.

Burchenal, J. H.; Murphy, M. L.; Ellison, R. R.; Sykes, M. P.; Tan, T. C.; Leone, L. A.; Karnofsky, D. A.; Craver, L. F.; Dargeon, H. W., and Rhoads, C. P.: *Clinical evaluation of a new antimetabolite, 6-mercaptopurine, in the treatment of leukemia and allied diseases*. *Blood* 8:963-999, Nov., 1953.

Balloon Technique in Detection of Cancer

Cytological examination of aspirated gastric contents has been advocated as a method for detecting early gastric cancer. Although Cooper reported more satisfactory gastric diagnostic specimens obtained by an abrasive-balloon technique, the method must not only determine accurately the presence or absence of cancer but must be readily acceptable to relatively well people to be of use as a cancer-screening test. Seventy-one patients with digestive symptoms but no known gastric cancer were advised to have cytological studies of the stomach contents. Of the

sixty-five patients who presented themselves, four refused to undergo the procedure without trying it, nine tried and then refused to complete the test, eleven co-operated but could not swallow the balloon. The time required to obtain a single gastric specimen varied from one to two hours and the total time consumed in completing one study was estimated to range from two and one-half to seven hours. Subsequent to the completed study each patient was given an upper gastrointestinal roentgen-ray examination with barium, requiring ten to twenty-five minutes. There was one false negative and one false positive produced by the abrasive-balloon technique. It is concluded that the procedure produces highly satisfactory cytological specimens but is not readily accepted by patients and is prohibitively time consuming for routine detection.

Chapman, D. L. S.; Klopp, C. T., and Platt, L. I.: Application of balloon technique in detection of cancer. Cancer 6:1174-1176, Nov., 1953.

Chronic Ulcerative Colitis

The development of malignant lesions in longstanding cases of chronic ulcerative colitis has been noted in a sufficiently large number of cases to mark it as a premalignant lesion. Of eighteen surgically treated patients with chronic ulcerative colitis, the author reports two cases of carcinoma. These patients, 47 and 56 years of age respectively, suffered from chronic ulcerative colitis for an average of thirteen and a half years before the onset of malignant transformation. They had experienced numerous acute exacerbations since onset and noted changes in their symptoms consisting in rectal fullness, frequent stools containing blood and mucus, and occasional constipation. They showed evidence of neoplasm on sigmoidoscopic tissue biopsies. Both had associated adenomatous polyps. The tumors in both cases were of a high grade of malignancy. As a result of this study the author recommends that the physician be on the lookout for complications including obstruction, perforation, perirectal abscess, polyposis, and malignant change as

soon as the diagnosis of chronic ulcerative colitis has been confirmed. Symptoms suggestive of carcinoma are unusual bleeding, prolonged local pain, change in number of stools, and weight loss. There is considerable controversy concerning the roles of various types of polyps thought to be responsible for the malignant changes occurring in the chronically infected lower gastrointestinal tract.

Hurt, L. E.: The relationship of chronic ulcerative colitis to malignancy. Ann. Surg. 139:838-843; disc. 843-845, June, 1954.

Prostatic Cancer

Early diagnosis based on careful palpation of the gland is the clue to complete surgical extirpation and cure of cancer of the prostate. In the earliest stages, prostatic cancer is asymptomatic. Unless benign hyperplasia of the gland also exists, urinary symptoms do not appear until the growth is relatively extensive and all chance of complete surgical extirpation is lost. In the vast majority of patients in the author's series who have survived five or more years following radical perineal prostatectomy, diagnosis was made by the discovery of an area of suspicious induration on rectal palpation. Under such circumstances the patient is prepared for the radical operation and the diagnosis is confirmed by exposure of the suspicious area and frozen-section biopsy. The suppression or withdrawal of androgen stimulation either by orchectomy or estrogen administration, enhances the success of radical prostatectomy. Androgen suppression causes regression of the tumor, presumably by destroying the neoplastic cells at the periphery of the growth. Unfortunately, cells at the point of origin are affected little, if at all, so that cure of the malignant growth by hormonal means is not possible. For advanced disease, androgen suppression should be used until effectiveness is lost, as evidenced by increase of local growth, onset of urinary symptoms, or metastases. Orchectomy should then be performed. Later additional suppression may be gained by adrenalectomy. The use of radioactive isotopes is still in

an experimental stage and requires further evaluation.

Colston, J. A. C.: *Diagnosis and treatment of carcinoma of the prostate; with special reference to the radical operation*. Pennsylvania M. J. 57:517-525, June, 1954.

Oral Cancer

Fourteen per cent of all cancer deaths in the United States are due to cancers of the head and neck. Nine per cent are due to mouth cancer. The incidence of mouth cancer is four males to one female. Several associated and predisposing factors in the etiology of mouth cancer are trauma from ragged, sharp teeth and malfitting dentures, chemical irritation from tobacco, poor oral hygiene, syphilis, pre-existing leukoplakia, and a hereditary tendency. The physician and dentist should stress the importance of good oral hygiene and dental care. Medical, dental, and lay educational propaganda, however, has tended to shorten the interval from first symptoms to diagnosis. Prerequisites for diagnosis are good illumination, adequate exposure, intraoral and bimanual palpation, and biopsy, which should be repeated if necessary. Patients often delay in seeking treatment because of absence of pain or bleeding, ignorance, and fear. A cancer of the mouth may be small and infiltrative or large and vegetative. It is firm to palpation and bleeds easily with trauma. The low-grade squamous-cell cancer is the most common form of mouth cancer. Adenocarcinoma is much less common, while sarcoma and malignant melanoma are extremely rare. Choice of treatment is very important. The relative merits and indications for different types of treatment are enumerated. Deep roentgen-ray therapy is generally considered the treatment of choice in tumors of the tonsil and base of the tongue. Inadequate or "palliative" dosage of roentgen rays is worse than none at all. Radiotherapy, however, is not the whole answer to the problem of oral cancer. Antibiotics, improved anesthesia, adequate blood replacements, and new and improved surgical techniques have helped patients who were previously thought hopeless. Adequate preparation,

good anesthesia, and proper postoperative care should take care of most medical contraindications to operation. Age should not be a deterrent. Patients with advanced cancer of the mouth should not be considered hopeless but should be offered the benefit of radical surgery. Eight illustrative case reports are presented.

Cummings, G. O., Jr.: *Cancer of the mouth*. J. Maine M. A. 43:140-145, May, 1952.

Carcinoma of the Parathyroid

Grossly, carcinoma of the parathyroid may be diagnosed if there is local invasion of the surrounding tissues or metastatic disease and strongly suspected if more than one mass is present or if the presenting mass is large. Microscopically, cellular pleomorphism, giant nuclei, nests of tumor cells in blood vessels, or apparent invasion of the capsule are not sufficient evidence for differential diagnosis of parathyroid tumors. Mitotic figures, a trabecular pattern, tumor thrombi, and lymphatic invasion are reliable criteria. Patients with parathyroid cancer average 41 years of age and are slightly younger than patients with adenoma. While adenoma is more common in women, the sex ratio is about equal with carcinoma. The usual presenting symptoms are those of hyperparathyroidism, and typical bone lesions can be seen in almost all cases. However, renal symptoms secondary to stone formation were found in only 25 per cent of patients before surgery, as opposed to the much higher incidence with adenoma. Renal calcinosis ultimately occurs with most cases of cancer. The patient usually has sharp pains in the bones secondary to osteoporosis. Roentgenological studies often demonstrate cystic bony lesions and renal calcifications. Physical examination may reveal a nodule in the neck. The serum calcium is elevated, and blood and pus will be noted in the urine if stone formation is prominent. If invasion by carcinoma of parathyroid is present at the original operation, it is imperative to remove all the tumor by radical surgery, and a radical neck dissection of the involved side should be considered. Irradiation

should be tried if complete excision cannot be accomplished.

Black, B. K.: Carcinoma of the parathyroid. Ann Surg 139:355-363, March, 1954.

Radioactive Isotopes

Radioactive isotopes are considered of greater use for diagnostic tests and laboratory investigations than for specific cancer therapy. I^{131} is useful for studying the metabolism of iodine and functions of the thyroid gland, but only 10 to 20 per cent of thyroid cancers are amenable to isotope therapy. Surgery remains the preferred treatment for most nodular goiters and for some localized and non-iodine-absorbing tumors. For treatment of hyperthyroidism, the present trend is toward a single large exposure with very active material to avoid the effects of long-term radiation therapy. Use of repeated small doses for periodic functional evaluations increases the possibility of cell aberration. P^{32} is advisable for polycythemia vera, particularly in the late stages. Au^{198} is promising for treatment of fairly well-localized cancer of the prostate gland. Special training in methods of local administration is needed, however. The most useful isotope is Co^{60} , a supervoltage therapeutic agent. For maneuverability, flexibility, and intensity of output, Co^{60} cannot be approached by other methods of equal power. Skin manifestations with supervoltage therapy are slight.

Harvey, R. A.: Observations in atomic medicine; the Carman Lecture. Radiology 62:479-487, April, 1954.

Cancer of Colon and Rectum

Of the 171,171 cancer deaths that occurred in the United States in 1941, 29,000 were caused by cancer of the bowel. In an effort to clarify some of the problems presented by this type of cancer, a statistical study has been made on 197 cases of cancer of the colon and rectum encountered during the three-year period from 1947 to 1949 inclusive at the Allentown General Hospital. Surgical treatment was employed in 165 of these patients; that is, the operability rate was 83.7 per

cent. The over-all survival rate of 28 per cent is discouraging. It is believed to be due to delay on the part of the patient in seeking medical advice. The cases of the patients undergoing extirpation of the rectum were reviewed in an effort to determine the five-year-survival rate. Six of the eighteen cases (33.3 per cent) are living and well today. The cases in a similar but larger group with operations performed in 1948 showed a four-year-survival rate of 43 per cent. It is probable that this increase in survival rate will continue from year to year. In discussing the basic problems involved in cancer detection and treatment, it was felt that cancer education, emphasizing the value of digital and proctoscopic examinations as a means of detecting precancerous, asymptomatic adenomatous polyps and early carcinoma, should be encouraged.

Kratzer, G. L.: Collective review of cancer of the colon and rectum in a general hospital. Am. J. Surgery 86:523-526; disc. 526-529, Nov., 1953.

Carcinoma Involving the Esophagus

At the Presbyterian Hospital in New York City 228 patients with carcinoma involving the esophagus were treated in the ten-year period from 1941 through 1950. Of these, 162 had primary carcinomas of the esophagus; forty-seven had carcinomas of the stomach with extension to the lower esophagus; and nineteen had carcinoma involving the esophagus but originating in some other structure. Most of the patients were in the sixth and seventh decades of life, and the ratio of men to women was approximately 4 to 1. No patient has survived five years after resection of a primary carcinoma of the esophagus. No patient lived more than one year after involvement of the esophagus in carcinoma originating in another structure other than the stomach. Improvements in operative techniques have resulted in substantial decrease in operative mortality during the second half of the period studied and may result in a higher proportion of long-term survivors, especially if greater selectivity is exercised in resorting to resection. Whether resec-

tion for palliation in cases with demonstrable irremovable metastases is justifiable as compared to results of radiotherapy remains in doubt. The authors feel that in order to achieve reliable evaluation of the therapeutic methods for this highly fatal disease, the results in unselected series rather than in series selected for operability should be reported.

Humphreys, G. H., II, and Moore, R. L.: *Carcinoma involving the esophagus*. *S. Clin. N. America* 33: 389-400, April, 1953.

Gastric Polyps Accompanying Cancer

A study of the pathological changes found in forty-five patients with gastric polyps, all but three cases representing autopsy material, is presented. Thirty-four of these patients had a total of fifty-three malignant tumors elsewhere (not unexpected, since the material was from institutions having a high rate of cancer at autopsy). Thirteen patients had more than one cancer for a total of thirty-three cancers in this group, or an average of 2.5 per case. The sites of cancer fell into three groups: twenty-five in the gastrointestinal tract, seventeen in endocrine target organs, eleven in a miscellaneous group. Pathological changes were observed in many of the endocrine organs, including eosinophilic hyperplasia or adenoma in seven of ten pituitaries examined. It is suggested that the formation of gastric polyps may be influenced by hormonal imbalances and that endocrine hyperfunction may be etiologically implicated in the cancers observed.

McManus, R. G., and Sommers, S. C.: *Significance of gastric polyps accompanying cancer*. *Am. J. Clin. Path.* 23:746-757, Aug., 1953.

Surgical Treatment of Cystic Lymphangioma

This report of eight cases of cystic lymphangioma urges simple surgical excision as the treatment of choice, even for the very large lesions that may require multiple operations. All but one of these patients were less than 2 years of age at the time of treatment. The case of a 6-week-old infant with a large cervicoaxil-

lary hygroma that was cured, with good functional result, after a two-stage resection is described in detail. All eight cases were operated on within fourteen months of the discovery of the lesion. Six have remained free of recurrence in a follow-up of more than two years; if these lesions recur, they usually do so within one year. One patient had two recurrences but has been free of recurrence since the third operation. Irradiation and sclerosing agents were used in but one case and are not recommended for use prior to surgery. A brief discussion of the pathogenesis of hygroma is included.

Freeman, G. C.: *Conservative surgical treatment of massive cystic lymphangioma; with the report of eight cases*. *Ann. Surg.* 137:12-17, Jan., 1953.

Carcinogen Tests

Skin changes resulting from the application of carcinogenic compounds may provide a rapid means for estimating species susceptibility. Loss of hair, suppression of sebaceous glands, and enlargement of nucleoli in epidermal cells were observed in the skins of mice and rabbits within ten days after painting with several carcinogenic materials. Rats and guinea pigs appeared more resistant to the carcinogenic compounds. In experiments on human skin, test materials were painted daily on areas of 1 sq. cm. of the upper back for four consecutive days. Biopsies made on the sixth day showed enlargement of nucleoli after coal tar or 3,4-benzopyrene, slight nucleolar enlargement after cigarette-smoke condensate or turpentine oil, and no effect on nucleoli after white mineral oil, which is known to be noncarcinogenic for mice. Sebaceous glands were not suppressed.

Rhoads, C. P.; Smith, W. E.; Cooper, N. S., and Sullivan, R. D.: *Early changes in the skins of several species, including man, after painting with carcinogenic materials*. [Abstr.] *Proc. Am. A. Cancer Res.* 1(2):40, April, 1954.

Public Opinion on Cancer

In the Manchester (England) area a survey was made of women's opinion and general knowledge concerning cancer in order to learn why they delay seeking ad-

vice for symptoms they suspect to be cancer. More than 50 per cent of the women reporting for treatment of cancer of the breast or uterus had delayed for more than three months, and 21 per cent for more than a year after first noticing symptoms. More than half the women thought cancer incurable. This misconception was a prominent cause for delay and shows the need for education. Cancer of the cervix occurs predominantly in the lower social groups in which ignorance of the symptoms is greatest. A lump in the breast is quite generally recognized as possible cancer, but there is no sense of urgency when cancer is so widely believed to be incurable. Women are interested and must be told of the good results that are possible when cancer of the breast and of the cervix are treated in an early stage. The responsibility of patients for seeking immediate advice must be constantly reiterated.

Paterson, R., and Aitken-Swan, J.: Public opinion on cancer; a survey among women in the Manchester area. Lancet 2:857-861, Oct. 23, 1954.

Cobalt 60 and Radium

Identical plaques of radium 226 and cobalt 60 applied to similar areas of skin on rabbits cause slight variations in irradiation effects but no significant differences in speed of reaction when dosage is calculated by Paterson-Parker converted tables. The two qualities of radiation were compared after plaques of the different modalities were placed on the opposite sides of the abdomens of rabbits and a total dose of 7000 gamma roentgens was delivered to a depth of 0.25 cm. on each side. Irradiation effects, including primary erythema intensity and area, induration, moist erythema intensity, primary healing, character, size, and secondary breakdown of scar were compared. Of fifty-eight rabbits so treated, thirty showed identical reactions from both modalities, twenty-seven had slightly more severe effects from cobalt 60, and only one had a

more severe reaction from radium. The rate of reaction was identical in thirty-three rabbits, faster with radium in thirteen, and faster with cobalt 60 in twelve. With the use of Paterson-Parker tables, a dose of 6000 to 6500 r with cobalt 60 in five to seven days may be more desirable than 7000 r with radium in interstitial and intracavitary or plaque techniques.

Meschan, I., and Nettleship, A.: Comparative effects of cobalt 60 and radium when utilized in identical doses on the skin of rabbits. Am. J. Roentgenol 71:306-319; disc. 330-332, Feb., 1954.

Diagnosis of Lesions of the Colon

While barium-enema examinations are often of definitive help in making a diagnosis, they can cause irreparable harm by engendering a false sense of security if mistakenly reported negative. Valuable time is lost before a subsequent operation, during which interval the lesion may have progressed to hopeless inoperability. Existing neoplasms of the colon are not shown in 5 per cent of barium-enema studies, and, if polyps are included, the number is closer to 15 per cent. Incomplete preparation of bowel, with consequent gas and feces and, occasionally, spasm, may produce an area interpreted as an organic lesion. Rectal growths up to 8 in. from the anal margin can escape roentgen-ray detection relatively easily, but these should practically all be felt with the examining finger or be visible through the sigmoidoscope. Lesions in the sigmoid and, less often, those around the splenic flexure may be missed both by the fluoroscope and in roentgenograms no matter how the patient is manipulated or turned. Emphasis is placed on roentgenographic examination of the colon as a diagnostic aid that must fit into the clinical picture as a whole to effect success in the treatment of cancer of the large bowel, which is dependent on early diagnosis.

Finney, J. M. T., Jr., and Stone, D. H.: The fallibility of roentgenograms in diagnosing lesions of the colon. Ann. Surg. 137:674-680; disc. 681-682, May, 1953.



a glance . . .

**one-minute abstracts
of the current literature
on cancer . . .**

Etiological Factors in Uterine Cancer

The author's study of seventy-five patients with cervical cancer, 293 with breast cancer, 125 with other types of cancer, and of 625 control persons without cancer (all patients and controls chosen at random) revealed that cervical carcinoma occurs with undue frequency among married women who have begun their childbearing at an earlier age than women without cervical cancer; among those who have had an average of three pregnancies before the woman with no cervical cancer has her first, and among those who continue to have offspring as late as, or later than, the average woman, thus producing large families. The most striking point of difference between the patients who have cervical carcinoma and those who do not is the age at which they begin their pregnancies. Compared with control women of the same parity, they have an average age of pregnancy significantly lower than that of the control women. This indicates that parity is not so important a factor as early childbearing. The series of patients with cervical cancer is too small to obtain evidence for or against a genetic basis, but the physiological experiences of reproduction seem

to have more significance than do the genetic factors. On the other hand, carcinoma of the fundus seems to have a definite genetic basis, which may be ascribable to hormones or tissues or to both. It appears to be associated with mammary cancer in some way, for relatives of fundal-cancer patients have a far-greater than expected frequency of mammary cancer than of cancers of other organs (if they have cancers at all). Further research is urgently needed concerning the roles, if any, played by the hormones of pregnancy, the effect of frequency of intercourse, the effect of parity on age of onset, and the role of lacerations of the cervix by childbirth.

Macklin, M. T.: Etiologic factors in carcinoma of the uterus, especially the cervix. J. Internat. Coll. Surgeons 21:365-378, Mar., 1954.

Carcinoma of the Corpus

Of 246 women with cancer of the body of the uterus treated at the Sloane Hospital for Women in New York between 1938 and 1948, fifty-seven received intracavitary radium therapy with or without subsequent roentgen-ray irradiation. Sixty-two were subjected to some type of surgical treatment with or without irradiation, and 127 were treated by preoperative

radium followed six to eight weeks later by hysterectomy. Of the fifty-seven patients, thirty-nine were followed up, and thirteen (33.3 per cent) of these obtained a five-year cure by radium; four of these thirteen patients had recurrences later, one of them after ten years. From these analyzed statistics, it appears that only 5 to 10 per cent of the cases of cancer of the body of the uterus are highly fatal, metastasizing probably before the disease is clinically manifest. Cancer of the body of the uterus in most cases remains localized in the uterus for a long time and is cured either by surgical intervention alone or by intracavitary radium therapy followed by surgical intervention. The mortality rate is higher among patients who do not show any response to irradiation than among those who do reveal a radiation response.

Corscaden, J. A., and Tovell, H. M. M.: The management of carcinoma of the corpus. Am. J. Obst. & Gynec. 68:737-756; disc. 756-760, Sept., 1954.

Therapy of Cervical Carcinoma

Considerable controversy exists concerning the value of radiation therapy of cancer that has already extended to regional lymph nodes. During the past decade a few surgeons in this country returned to the radical Wertheim operation combined with regional lymphadenectomy for the treatment of certain early selected cases of cervical carcinoma. The reasons for this return to the surgical approach were: (1) the prevention of recurrence or reoccurrence locally by removal of the cervix; (2) the fact that certain tumors are radiation-resistant, (3) the hope of salvaging a certain percentage of patients who already have lymphnode metastasis, and (4) the avoidance of untoward radiation injuries to surrounding structures. The author's experience with radical hysterectomy leads him to believe that the survival rate is not greater than that obtained by proper radiation therapy in cases of similar extent. Exploratory laparotomy combined with regional lymphadenectomy should constitute the first step in the therapy of cervical carcinoma followed by

full external roentgen-ray therapy and the local application of radium into the cervical canal and into the lateral vaginal vaults. Present methods of applying radium plus the roentgen-ray dosage yield an estimated cancerocidal dosage to structures 4 cm. distant from the mid-line. Therefore the author depends upon the local application of radium to destroy the original lesion and on the combination of lymphadenectomy and external roentgen-ray therapy to eradicate the disease along the lateral walls of the pelvis.

Kimbrough, R. A., Jr.: Therapy of carcinoma of the cervix uteri. Pennsylvania M. J. 57:732-734, Aug., 1954.

Estrogens in Cervical Carcinoma

The results of the use of large doses of diethylstilbestrol for palliative therapy of carcinoma of the cervix uteri are described. Stilbestrol administered orally in doses of 25, 50, and 100 mg. daily apparently has a hemostatic effect in cases of advanced cervical carcinoma with profuse bleeding as well as a powerful action on tissue epithelialization. The hemostatic effect appears to be more rapid in patients who have not previously received radiation therapy. Patients with tissue necrosis and extensive local infection, regardless of whether they had been previously irradiated, appeared to escape the effect of stilbestrol. Biopsies taken at repeated intervals in cases of invasive carcinoma revealed presence of cancer, although notable changes had occurred under the influence of estrogenic action. Diethylstilbestrol, although no cure for cervical carcinoma, affords palliation to the extent that many patients experienced subjective improvement, gaining the impression that a cure has been effected.

Nieburgs, H. E.: The effect of excessive doses of diethylstilbestrol on carcinoma of the cervix. Obst. & Gynec. 2:213-229, Sept., 1953.

Carcinoma of the Cervix

The recent revival of interest in this country in the surgical treatment of carcinoma of the cervix uteri has raised the question of whether surgery or radiation is

the better method of therapy in this disease. To evaluate these modalities, fifteen patients with early cervical carcinoma treated by radical surgery were matched case for case with a similar series of fifteen patients treated by radiation at the same institution and during the same period of time. In using this technique, two patients treated by different methods are matched for as many as possible of the characteristics likely to cause variation in response, each pair representing a separate experiment. Surgical treatment consisted of radical panhysterectomy with removal of the parametria, upper vagina, and iliac and obturator lymph nodes. In the fifteen radiation cases treatment consisted of a course of roentgen-ray radiation followed by radium application to the cervix. The effect of variations in technique was that radiation treatment tended to be more nearly ideal than surgical therapy. (Most of the radiation was administered by one gynecologist; surgery was done by seven surgeons, none operating on more than five cases.) If both methods were equally effective, the results obtained by surgery in this series might have been expected to be worse than those obtained by radiation, but this was not the case. There was little difference between the two groups, over an average follow-up period of twenty-six months, in survival, recurrence of disease, or the incidence of early or late complications of treatment.

Newton, M.: Carcinoma of the cervix: use of matched pairs of cases to compare treatment by surgery or radiation. Surg., Gynec. & Obst., 99:29-33, July, 1954.

Radioresistant Cervical Cancer

Radiation is generally recognized as the proper treatment for cancer of the cervix, but surgical excision has a definite use, especially in cases of radiation failure. Prompt biopsy confirmation of radioresistance would be especially desirable but is beset with such technical difficulties that correlation of radiation histology and prognosis has been impossible up to the present. Twelve radiation failures with subsequent radical surgical treatment are analyzed. Previous impressions are re-

affirmed as to the relative resistance of the spinal type of tumor, but the study suggests that pure tumor strains are rare, and degree of differentiation in the accepted sense does not parallel neoplastic tendencies. Broders's plan for grading according to cellular activity seems a more reliable guide than one based solely on degree of differentiation. The patchy localized response to irradiation is one of the most striking variables and further emphasizes the probability that random biopsy alone can never be the criterion of tumor behavior after treatment.

Novak, E. R.: Radioresistant cervical cancer. Obst. & Gynec. 4:251-259, Sept., 1954.

Endometrial Biopsy

The author concludes that endometrial biopsy should be utilized as a diagnostic technique in malignant diseases of the uterine corpus. The findings in a study of 445 women (more than 35 years of age) with irregular uterine bleeding show that adenocarcinoma of the endometrium was present in ninety-five of these patients and the cancer was diagnosed by endometrial biopsy only in ninety-two cases. Endometrial biopsy offers a means of establishing an earlier diagnosis to counterbalance other unalterable handicaps encountered, as a rule, in women who develop adenocarcinoma of the endometrium. Endometrial biopsy is useful in localizing the tumor and is a means by which combined adenocarcinoma of the uterine body and cervix can be differentiated from true primary adenocarcinoma of the cervix. The plan of treatment can be altered accordingly.

Wall, J. A.; Fletcher, G. H., and MacDonald, E. J.: Endometrial biopsy as a standard diagnostic technique: a review of 445 cases. Am. J. Roentgenol. 71:95-101, Jan., 1954.

Pelvic Venography

Roentgenographic visualization of the principal pelvic veins aids in the diagnosis, estimation of prognosis, and in the treatment of cancer of the female genital tract. The nature and site of obstruction of the major pelvic vessels can be determined by

pelvic venographic examination, since the films demonstrate collateral circulatory systems of the pelvis. Lymphatic and venous occlusion as causes of edema of the legs can be differentiated by this procedure. Also, pelvic lymph-node areas can be localized when radiotherapy is contemplated. A correlation exists between peripheral edema and the status of the pelvic venous system. Edema of a lower extremity can be attributed to venous blockage only in the absence of good collateral circulation. If an adequate collateral circulation can be demonstrated, the edema must be attributed to inflammatory changes or lymphatic obstruction or both.

Dalall, S. J.; Plentl, A. A., and Bachman, A. L.: *The application of pelvic venography to diagnostic problems associated with cancer of the female genital tract*. *Surg., Gynec. & Obst.* 98:735-742, June, 1954.

Cervical vs. Corpus Cancer

Three hundred ninety cases of primary carcinoma of the uterus are reviewed with the purpose of correlating the frequency of carcinoma of the uterine corpus with that of carcinoma of the cervix. Although the concept that carcinoma of the cervix is from three to eight times more common than primary cancer of the uterine corpus is generally recognized and corroborated by previously published reports this study dissents from its clinical acceptance. In this series of 390 patients the ratio of primary cancer of the cervix to cancer of the uterine corpus was 1.08 to 1, or 51.8 per cent cervical cancer, and 48.2 per cent corpus cancer. Thirty-seven cases of carcinoma *in situ* of the cervix were not included as primary cancer of the cervix; categorized thus, the ratio of cancer of the cervix to primary carcinoma of the uterine corpus would be 1.30 to 1, or 56.4 per cent. Multiple factors considered to influence this change in ratio are: heightened cancer consciousness resulting in less patient delay, improved and routine office use of such diagnostic procedures as Schiller's test, colposcopy, vaginal and cervical smears, and biopsies increasing the number of early treatments, and accessibility in diagnostic examination and study of secretions. With in-

creased life expectancy, cancer of the uterine corpus is in greater evidence as a postmenopausal lesion.

Strand, C. M., and Wheelock, M. C.: *Ratio of cervical carcinoma to corpus carcinoma*. *Obst. & Gynec.* 4:380-382, Oct., 1954.

Cytological Detection of Uterine Carcinoma

One hundred cases of uterine carcinoma were detected in the routine cytological examination of 12,116 presumably well women at the Cancer Detection Clinic of the Los Angeles Cancer Prevention Society during the years 1952 and 1953. Of these, eighty-nine were squamous cancers of the cervix, fifty-two of which were estimated to be early (asymptomatic) and therefore should yield a high percentage of cures. The absence of clinical symptoms and signs in early uterine cancer makes it advisable that all patients presenting themselves for a cancer detection examination have Papanicolaou smears. Negative vaginal smears are not a substitute for sound clinical judgment in the management of the patient with abnormal bleeding. Some cases showed abnormal cytological changes that probably represented a stage in cervical carcinogenesis, intermediate between benign hyperplasia and carcinoma, for which the term "dysplasia" is suggested. Adequate biopsy including curettage, where indicated, should be done on all cases with positive cytology. Biopsy confirmation establishes the stage, grade, and type of cancer so that a wise choice of therapy may be made.

Stern, E., and Menoher, N. P.: *Cytologic detection of uterine cancer; in a cancer detection clinic*. *J. Am. M. Women's A.* 9:343-349, Nov., 1954.

Ovarian Tumors Complicating Pregnancy

The possibility of cancer in ovarian tumors complicating pregnancy must always be considered. More than a third of ovarian tumors are misdiagnosed during pregnancy and in the postpartum period. With a careful bimanual pelvic examination, most adnexal masses can be palpated in the first trimester. During the second

trimester an ovarian tumor can usually be palpated as a separate mass from the enlarging uterus. Roentgenograms of the abdomen may aid in differentiation of tumors. A mass outside the uterus with displacement of the fetal head, teeth or calcification in dermoid tumors, or a large mass not containing a fetal skeleton will often establish or confirm the diagnosis. Surgery should be performed in the first trimester when an acute abdominal crisis seems evident. In the second trimester, an adnexal lesion that becomes increasingly tender or an asymptomatic tumor that is 6 cm. or larger in diameter also will require operation. After surgery in the first or second trimester, the patient may be allowed to continue the pregnancy and be delivered vaginally without fear of wound disruption. If an ovarian tumor 8 cm. or larger is found obstructing the birth canal near term, cesarean section should be performed and the tumor removed. No deaths occurred among forty-five women as the result of ovarian-tumor surgery.

Gustafson, G. W.; Gardiner, S. H., and Stout, F. E.: *Ovarian tumors complicating pregnancy: a review of 45 surgically proved cases*. Am. J. Obst. & Gynec. 67:1210-1220; disc. 1220-1223, June, 1954.

Preinvasive Carcinoma of the Cervix

Seventy-one women between the ages of 20 and 61 years with preinvasive carcinoma of the cervix uteri (carcinoma *in situ* or intraepithelial cancer) were studied to correlate the findings in different types of cervical biopsies with those of subsequent hysterectomies. Twenty-five of these women had residual cancer in the uterus subsequent to biopsy. Thirty-eight patients had small or superficial biopsies, and thirty-three had large, thick-cone biopsies. Residual carcinoma was found in the hysterectomy specimens of sixteen of the thirty-eight patients as compared to nine of the thirty-three patients. At least minimal but definite involvement of glands was found in sixty-five of the seventy-one patients. The extent of glandular involvement could be fairly well estimated in thick-cone biopsies, while in small biopsies the hysterectomy specimen had to be correlated in order to accomplish such esti-

mate. The thick-cone biopsy, therefore, is the method of choice in every patient with a positive vaginal smear or clinical suspicion of cancer. In selective cases, the thick-cone biopsy may by itself constitute definitive treatment but should then be followed by periodic vaginal smears.

Huey, T. W., Jr.; Large, H. L., Jr., and Kimmelstiel, P.: *Preinvasive carcinoma of the cervix: correlation of findings in biopsy and hysterectomy specimens*. Am. J. Obst. & Gynec. 68:761-768, Sept., 1954.

Total Hysterectomy

Complications that sometimes arise from a cervical stump after incomplete hysterectomy make total operation preferred unless definite contraindications exist. In the genetically predisposed patient, cervical irritations may favor production of carcinoma of the cervix, and stump infections may frequently cause pelvic pain, leukorrhea, bloody discharge, and dysuria. Definite lesions were found in 63.6 per cent of cervixes removed during 800 total abdominal hysterectomies for benign disease. Benign polyps left in a cervical stump almost always cause bleeding. Although there is considerable disagreement as to the influence of benign cervical lesions on the development of cancer, many regard squamous metaplasia and basal-cell hypertrophy as precursors of carcinoma.

Wesley, R. H.: *A study of cervices removed at total hysterectomy for benign disease*. Am. J. Obst. & Gynec. 67:293-296, Feb., 1954.

Primary Carcinoma of the Vagina

In most respects, the manifestations of carcinoma of the vagina resemble those of malignant growth in the cervix. The early lesion is asymptomatic. Painless bleeding is the most frequent symptom and is often the first indication. The condition must be differentiated from the much more common secondary cancer of the vagina. The author concludes that the best therapy for primary vaginal cancer is local irradiation by either surface applicator or interstitial needles of radium. Subsequent roentgen-ray therapy may be used. Difficulties of treatment are not due

to inaccessibility or radioresistance of the lesion but to the radiosensitivity of the bladder and rectal mucosa. Technique and dosage must be planned for each individual because of the extreme variations in position and type of the cancer.

Palmer, J. P., and Biback S. M.: Primary cancer of the vagina. Am. J. Obst. & Gynec. 67:377-397, Feb., 1954.

Detection of Cancer of the Cervix

In a period of four years, 17,267 smears of material scraped from the cervix of patients observed in private practice were examined. Of that total, 11,207 were from women who had not previously had examination of smears, and in 112 cases cancer was detected by the cytologic examination. In eighty of those cases cancer was not suspected until the slides were examined; in seventy-four of the eighty the growth was intraepithelial, in 6 in an early invasive stage. The smears are obtained during all routine pelvic examinations and are sent to a near-by clinical laboratory for appraisal by specially trained technicians. The expense of \$3.50 for preparing and examining one slide has been borne willingly by more than 11,000 women who were examined during the period of the study. Simplified Papainicolaou smear techniques appear to be adaptable to private clinical practice when experienced cytodiagnosis laboratory facilities are available. From their experience during a four-year period, the authors are convinced that cytological examination of a smear from the uterine cervix is a practical, desirable method for routine use in private practice.

Martin, P. L.; Slate, T. A., and Merritt, J. W.: Cytologic detection of cervical cancer: four years' experience with routine smear examination in private practice. California Med. 79:108-111, Aug., 1953.

Carcinoma of the Uterus

A discussion of the management of carcinoma of the uterus and its preinvasive and invasive forms is presented. It is recommended that conservatism be employed in the young woman with preinvasive cancer confined to the layers of the epi-

thelium if she desires children. Preinvasive carcinoma of the cervix with gland invasion requires hysterectomy. In pregnancy this lesion deserves watchful expectancy, with the use of all diagnostic methods and careful follow-up. Invasive carcinoma of the cervix can be treated successfully by irradiation in 40 per cent of the cases. Surgical therapy for invasive cancer of the cervix should be reserved for radiation failures. Endometrial carcinoma can be destroyed in 75 per cent of the cases by the use of the Y applicator of Schmitz to deliver 6000 mg.-hr. of radium within the uterine cavity, in addition to 4000 r of 1000-kv. roentgen rays delivered to the mid-pelvis. Changes in the endometrium, myometrium, blood vessels, and tumor cells indicate that such therapy can retard the spread of tumor cells, if still present.

Schmitz, H. E., and Gajewski, C. J.: Management of carcinoma of the uterus. S. Clin. North America 33:259-268, Feb., 1953.

Cervical Stump Carcinoma

Carcinoma of the cervical stump can and should be almost completely eradicated, according to this report of eighteen cases. The authors state that by the use of total hysterectomy, which is possible in practically all cases where removal of the uterus is indicated, cancer of the cervical stump can be made impossible and, in a few cases in which supracervical hysterectomy must be done, careful evaluation of the cervix by biopsy or by cytological studies will usually suffice as an adequate prophylaxis. Cervical-stump carcinoma gives a poorer prognosis than carcinoma of the cervix in an intact uterus because adequate radium therapy is more difficult owing to the short endocervical canal and proximity of the bladder. Moreover, a patient who has had a supravaginal hysterectomy often has a false sense of security and tends to ignore early symptoms of cancer. Nine, one half the total series, were listed as coincidental carcinoma, that is, present at the time of surgery or within one year thereafter. The remaining cases occurred more than one year following

surgery and were listed as sequential carcinoma. There was a total of eight deaths, six of which occurred in the coincidental group. Only one patient lived longer than one year following therapy. There were two survivals for more than five years, both of which were in the sequential group. Although the authors have treated carcinoma of the cervical stump by a combination of radium and roentgen-ray therapy, their plea is for total hysterectomy in preference to supravaginal hysterectomy and thorough search for carcinoma in all cases in which the cervical stump must be left intact.

Kelley, A. J., and Brawner, D. L.: Experience of the Savannah Tumor Clinic in carcinoma of the stump of the cervix. Am. J. Obst. & Gynec. 66:711-715, disc. 715-717, Oct., 1953.

Delayed Diagnosis of Pelvic Cancer

The need for positive action to promote earlier cancer detection led the Obstetrical Society of Philadelphia in 1945 to form a Committee for the Study of Pelvic Cancer. Patients known to have pelvic cancer are interviewed and a brief, concise, and uniform questionnaire is used to obtain information pertinent to the question of a delay period. At the present writing the data are cumulative from 1945 to 1952 and include 2765 living patients with pelvic cancer. Patient delay comprises the greatest cause of delay, more than twice that of physician alone, and more than twice that shared by physician and patient. A table presenting the sites involved and the various categories of responsibility in percentages compared with the 1950 report shows that, whereas two years ago physician delay was greatest in cancer of the vulva, the latter has been superseded by cancer of the cervical stump. Cervical stump cancer also leads in delay in the institutional column. The most frequent error of omission by the physician is failure to make a pelvic examination at the initial visit. Inadequate diagnosis demonstrated by symptomatic management of pruritus of the vulva, with or without associated leukoplakia or kraurosis, with a variety of measures both local and general often for so long a time that chronic

changes in the integument may disguise a discrete lesion, is also a responsible factor. In numerous cases either roentgen-ray or radium treatment has been employed to control so-called benign uterine bleeding without an accompanying diagnostic curettage or biopsy, and endometrial or even cervical cancer has thus been overlooked.

Scheffey, L. C.: The delay period in the diagnosis of pelvic malignancy. Obst. & Gynec. 1:554-563, May, 1953.

Delayed Treatment of Cervical Carcinoma

To eliminate the delay in treatment of carcinoma of the cervix, intensive studies should be made of the factors that contribute to patient and physician delay. A review of fifty-six patients with invasive carcinoma of the cervix treated at the North Carolina Memorial Hospital shows that in 43 per cent of the patients at least three months elapsed between the time the patient first noticed a symptom of cancer and the time she sought medical care, and that the greatest physician and patient delay occurred in nonprivate rural patients. In 33.8 per cent of the cases, the physician delayed at least one month in establishing the diagnosis of cancer. The largest number of stage-III and -IV carcinomas were in this group as well. The author concludes that the resistance of patients to pelvic examination, the administration of drugs without physical examinations, the cost of biopsy and cytological studies, and the paucity of medical facilities in some sections of the state contributed to the physician delay in diagnosis of cervical cancer.

Flowers, C. E., Jr.: Delay in treatment of carcinoma of the cervix. Bull. Univ. North Carolina School Med. 2:12-14, Oct., 1954.

Carcinoma of the Ovary

Early diagnosis by means of periodic pelvic examination is essential to increased survival, since, in carcinoma of the ovary, onset is insidious and, when symptoms appear, prognosis is poor. Symptoms of ovarian carcinoma are frequently mul-

tiple. Vague digestive and urinary disturbances may precede the more obvious complaints of abdominal swelling and pain, vaginal bleeding, and weight loss. Physical findings may not be apparent with malignant disease. The most frequent findings include ovarian mass, ascites, frozen pelvis, and pelvic nodulation. Metastases are common and may be the first indication of neoplasm. In a review of 262 cases of ovarian malignant disease from 1931 to 1952, most were either serous or pseudomucinous cystadenocarcinomas. The ages of the patients ranged from 13 to 104 years, with most of the patients being between the ages of 40 and 65. In the patients less than 30, malignant teratomas, dysgerminomas, and hormone-producing tumors comprised the majority of the neoplasms. Menstrual irregularity was reported in about 22 per cent of the patients. Although the infertility rate was somewhat higher than in the general popu-

lation, three patients with ovarian carcinoma were pregnant. Family histories were available for 213 of the patients; ninety-two of these reported carcinoma in other members of the family. Patient delay (averaging nine months), errors in diagnosis, and the silent nature of onset account for the advanced state of the neoplasm at the time of the original diagnosis. Analysis of treatment has suggested that total hysterectomy, bilateral salpingo-oophorectomy, and postoperative roentgen-ray therapy offer the best hope for survival. But the authors emphasize that only frequent periodic pelvic examination, coupled with a high index of suspicion directed at the susceptible age group, especially where there is a positive family history of malignant disease, can lead to earlier diagnosis—our only present hope for increased survival.

Pearse, W. H., and Behrman, S. J.: *Carcinoma of the ovary*. *Obst. & Gynec.* 3:32-45, Jan., 1954.

Notes from the American Cancer Society Annual Meeting

(See also NEWSLETTER)

Mckelvey (University of Minnesota) assigned to surgery a role in the treatment of early cervical cancers but not in advanced cases. He said extensive surgery may be "dangerous and deforming" and offers only a small possibility of cure for cases unresponsive to radiation. Incomplete surgery, which leaves some of the tumor within the patients, somehow alters the host's relationship to the tumor and shortens life expectancy, he added. Alternate radium and roentgen-ray treatment, applied as continuous therapy, has yielded cure rates of 80 per cent for stage I, 50 per cent for stage II, 30 per cent for stage III and zero for stage IV. In this course, stage-I and -II patients are given 3000 r over twenty-five treatment days, while stage-III patients are given 3500 r or more if they can take it in safety. He mentioned that another investigator at the University of Minnesota has found that local injections of hydrocortisone protect the bowel against radiation damage, probably by preventing the laying down of connective tissue.

Garcia (Charity Hospital, New Orleans) obtained his best results using both roentgen-ray and radium therapy, keeping the parametrial dose within specified limits, and delivering the largest possible paracervical dose. He advocated large fields for advanced lesions and low daily treatment doses for infected cases. His most recent salvage rate is 41 per cent, and he believes this will improve with increased control of tissue dosage.

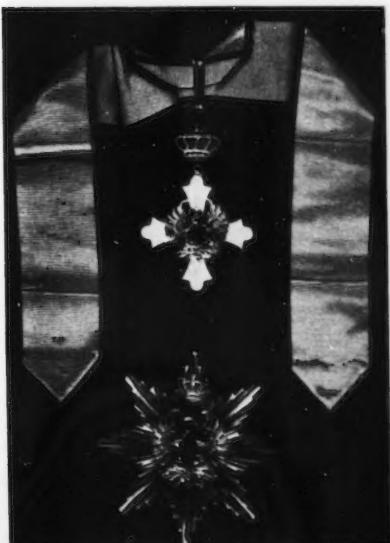
Dr. Papanicolaou Honored

King Paul of Greece, in a personal meeting at the Waldorf Astoria Hotel on December 3, 1953, presented to Dr. George Nicholas Papanicolaou the Cross of Grand Commander of the Royal Order of Phoenix.

In 1948 Dr. Papanicolaou received the Borden Award of the Association of American Medical Colleges and the Amory Award of the American Association of Arts and Sciences; in 1950, the Lasker Award of the American Public Health Association; in 1951, the First Award of the Order of AHEPA, as the most outstanding American scientist of Greek descent; in 1952, the American Cancer Society Award for Distinguished Service to Cancer Control; in 1953, the Wien Award and the Royal Order of Phoenix; and in 1954, the Modern Medicine Award.

Dr. Papanicolaou was born in Coumi (Euboea) Greece, May 13, 1883. He received his medical degree from the Uni-

Cross of Grand Commander of the Royal Order of Phoenix, presented to Dr. Papanicolaou, December 3, 1953, in New York, by King Paul of Greece.



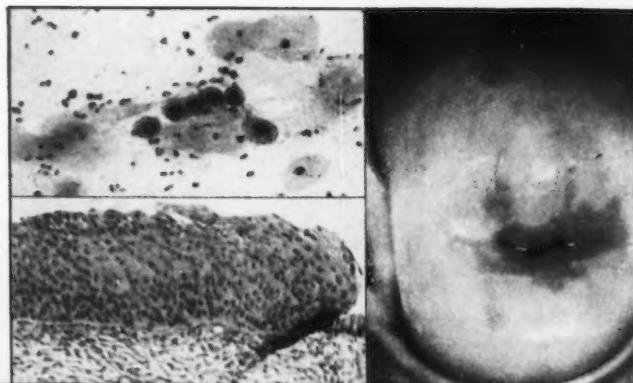
versity of Athens in 1904 and his Ph.D. from the University of Munich in 1910. In 1911 he served as physiologist in the expedition organized by the Prince of Monaco, and in 1912 and 1913 in the Medical Corps of the Greek Army during the Balkan War. In 1913 he came to the Department of Pathology of the New York Hospital. Since that time he has been Instructor and Associate Professor of Anatomy, and Professor of Clinical Anatomy of the Cornell University Medical College. He is now Emeritus Professor at Cornell and Consultant in Cytology at the Kate Depew Strang Cancer Prevention Clinic.

Dr. Papanicolaou's researches have been in the fields of anatomy, pathology, and endocrinology with special attention to the physiology of reproduction and the cytological diagnosis of cancer. He is the author of several books and more than a hundred articles on these subjects. His comprehensive *Atlas of Exfoliative Cytology* was recently published by Harvard University Press. He is a member, or corresponding or honorary member, of a score of American and foreign medical and scientific societies.

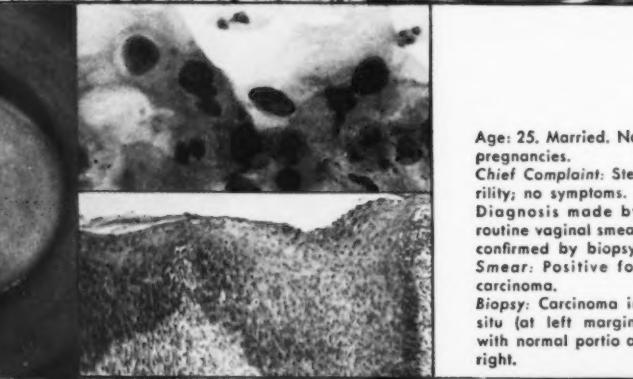
Dr. Papanicolaou is responsible for training of most of the leading cytologists in this country and abroad, squab Phoenixes flown from the fertile nest of the Grand Commander of this Royal Order of rare birds—the Master Cytologist.

Which Cervix Has the Cancer?

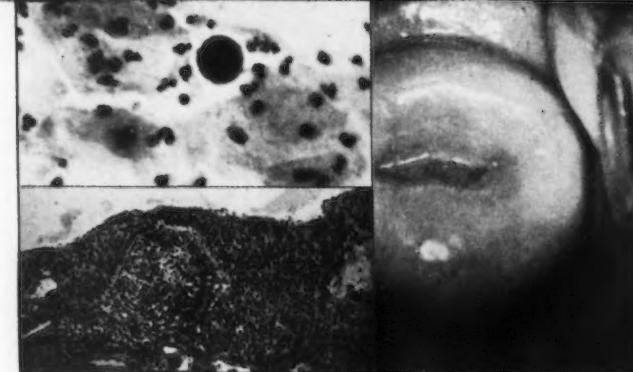
Age: 37. Married.
Three pregnancies.
Chief Complaint: Ab-
normal flowing,
bleeding, and spot-
ting, especially post-
coital; no leukorrhea.
Diagnosis made by
simultaneous smear
and routine biopsy.
Smear: Positive for
carcinoma.
Biopsy: Carcinoma in
situ.



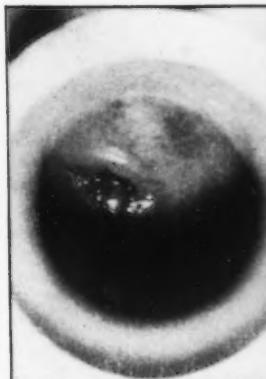
Age: 33. Married.
One pregnancy.
Chief Complaint: Ste-
rility; no pelvic symp-
toms.
Diagnosis made by
routine biopsy.
Smear: Probably pos-
itive for carcinoma
(original one re-
ported "suspicious";
subsequent ones,
"probably positive").
Biopsy: Carcinoma in
situ.



Age: 25. Married. No
pregnancies.
Chief Complaint: Ste-
rility; no symptoms.
Diagnosis made by
routine vaginal smear
confirmed by biopsy.
Smear: Positive for
carcinoma.
Biopsy: Carcinoma in
situ (at left margin)
with normal portio at
right.



Take Papanicolaou Smears Routinely!

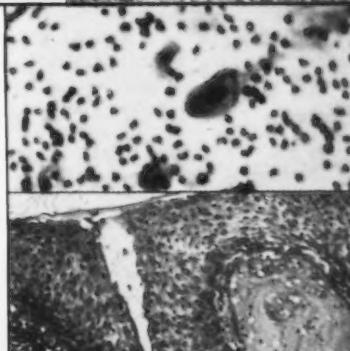


Age: 38. Married. No pregnancies.

Chief Complaint: One episode of metrorrhagia and one profuse period. Pelvic findings negative except for small, non-friable erosion, clinically not suspicious of cancer.

Smear: Cells "suspicious of malignancy."

Biopsy: Proliferative endometrium; carcinoma in situ of the cervix.

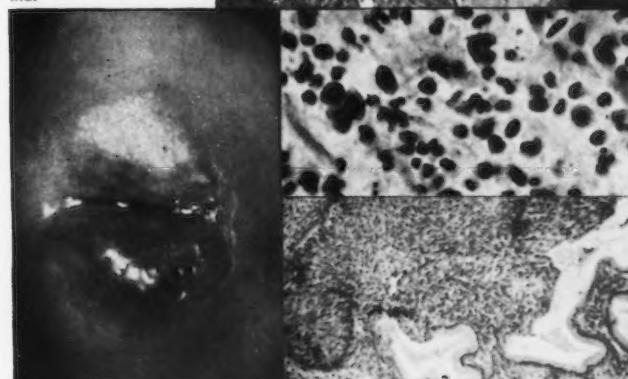


Age: 22. Single. No pregnancies.

Chief Complaint: Leukorrhea and bloody discharge for two weeks.

Smear: Atypical, benign.

Biopsy: Marked epidermoid hyperplasia, squamous metaplasia, and early leukoplakia.



Age: 26.

Chief Complaint: General weakness, loss of weight, persistent nervous tension, recurrent right lower-quadrant pain.

Smear: Many atypical cells; a few of early intraepithelial squamous-carcinoma type.

Pathological Diagnosis: Preinvasive carcinoma of the cervix (Bowen's disease).

Prospects for Improving the Cure Rate in Cancer of the Cervix

John B. Graham, M.D., and Ruth M. Graham

In recent years some progress has been made in the therapy of patients with cancer of the uterine cervix. These improvements lie in the rational selection of treatment and in better treatment itself.

Unfortunately, no form of management is infallible, and indeed the best rarely cures more than half of any unselected series. The patient in whom it is impossible to remove the tumor completely at the time of radical surgery might better have been treated with radiation, and the apparently early lesion that recurs locally in a few months after irradiation perhaps should have been excised. This retrospective type of reasoning receives some support from the SENSITIZATION RESPONSE (SR) observed in the vaginal smear.²

Some patients with cancer of the cervix show a characteristic change in the nonmalignant cells of the vaginal smear. This consists of a dense, finely vacuolated cytoplasm in the basal cells. The frequency of SR cells varies and can be determined by differentially counting 100 consecutive nonmalignant epithelial cells. The critical line is drawn at 10 per cent so that patients who have 10 per cent or more SR cells in the vaginal smear are said to have marked SR and those with 9 per cent or less have poor SR.

The term "sensitization response" is used because patients with marked SR appear to be especially sensitive to irradiation, and their tumors respond favorably. The five-year results in 136 cases of cancer of the cervix treated radiologically are presented in Table 1. The patients are

divided into two groups, those with marked SR and those with modest SR. The results are most striking in stage II, in which those with marked SR have a cure rate of 80 per cent (twenty-four of thirty), while those with poor SR show a cure rate of 23 per cent (eight of thirty-five). Stage-I and -III cases show the same trend in smaller numbers.

When the entire material is considered, the differences are pronounced, for of fifty-one with marked SR, thirty-seven (73 per cent) were cured; and of eighty-five with poor SR, only fifteen (18 per cent) were cured.

Somewhat surprisingly, the same prognostic significance does not apply in patients treated surgically. The apparent cure rate in 103 patients with stage-I and -II cancer of the cervix after radical hysterectomy and regional lymphadenectomy is indicated in Table 2. These were followed for two to five years and so are not precisely comparable with the irradiated series. However, the striking fact remains that of the twenty-three cases with marked SR, only nine (39 per cent) were cured, while fifty-seven (71 per cent) of eighty with modest SR were cured. This difference between the surgical and the irradiated results is particularly evident in Table 3. Those stage-I and -II cases with

TABLE 1
SR in Patients Treated Radiologically
—Five-Year Results

	10% or more SR		9% or less SR	
	No.	Cure	No.	Cure
Stage I	12	7	23	6
Stage II	30	24	35	8
Stage III	8	6	20	1
Stage IV	1	0	7	0
TOTAL	51	37 (73%)	85	15 (18%)

From the Vincent Memorial Hospital, the Gynecological Service of the Massachusetts General Hospital, Boston, Massachusetts.

The testosterone propionate used was generously supplied as Oretan by Schering Corporation, Bloomfield, New Jersey, and the α -tocopherol as Natoperol by Abbott Laboratories, North Chicago, Illinois.

TABLE 2
SR in Patients Treated with Radical Hysterectomy and Regional Lymphadenectomy—Two- to Five-Year Results

	10% or more SR		9% or less SR	
	No.	Cure	No.	Cure
Stage I	12	7	62	46 (74%)
Stage II	11	2	18	11 (61%)
TOTAL	23	9 (39%)	80	57 (71%)

marked SR treated radiologically showed a 74 per cent cure rate, and those with poor SR treated surgically showed almost the same cure rate (71 per cent). Obviously the selection of treatment in stage I and II on this basis would give a better net result.

The cytological response DURING radiotherapy is comparable to, but somewhat more precise than, SR. It is referred to as the radiation reaction, or RR.³ During the course of radiotherapy the nonmalignant epithelial cells of the vaginal smear undergo a series of changes: increase in cell size, cytoplasm vacuolization, multiple nuclei, and nuclear change. The proportion of nonmalignant epithelial cells exhibiting these alterations varies from patient to patient, with the amount of irradiation and time. The response is evaluated by differentially counting 100 consecutive cells; those showing radiation effect are expressed as a percentage and charted as in Fig. 4. If a patient shows radiation effect in 75 per cent or more, the response is regarded as favorable and she is said to have good RR. However, if a level of 75 per cent is not attained, the response is called poor and the prognosis is bad. The five-year results in 142 cases treated radiologically and evaluated in this manner are indicated in Table 4. As can be seen, those with good RR show a 65 per cent cure rate (fifty of seventy-seven), and those with poor RR a cure rate of only 8 per cent (five of sixty-five). These differences are apparent in all stages except IV, in which there were no survivors.

It is not really necessary to wait until the entire course of radiation has been

TABLE 3
Cancer of the Cervix—Stages I and II

	10% or more SR		9% or less SR	
	No.	Cure	No.	Cure
Radiation	42	31 (74%)	58	14 (24%)
Surgery	23	9 (39%)	80	57 (71%)

given, for one can accurately evaluate the response midway. If two applications of radium are the definitive treatment, the cytological response ten to fourteen days after the first radium exposure will indicate probable success or failure. Similarly, the response after 3000 r full pelvis roentgen rays in the region of the cervix will predict the outcome. It is virtually unknown for a patient to exhibit a poor response in the first half of her radiotherapy and subsequently to respond favorably to radiation alone. Thus, before the radiotherapy is half over, one can recognize most of the cases in which it will fail. At that point, some other method of treatment, such as surgery, may be elected, or an attempt may be made to make the irradiation more effective. One means of approaching the latter is to make the tumor more vulnerable, so that it will succumb more readily to the roentgen rays and radium.

The observation that changes in the nonmalignant epithelial cells are of importance in prognosis suggests one of two possibilities: either that the host and the tumor share a common sensitivity to irradiation or that the host response to irradiation is a major factor in the control of the cancer. Either or both of these may apply. A change in the patient's sensitivity

TABLE 4
Cancer of the Cervix Treated Radiologically—Five-Year Results

	Good RR		Poor RR	
	No. Cured		No. Cured	
Stage I	13	9	2	0
Stage II	45	35	24	3
Stage III	15	6	26	2
Stage IV	4	0	13	0
TOTAL	77	50 (65%)	65	5 (8%)

to irradiation should be reflected in a parallel change in the response of the tumor. If the patient could be made more sensi-

tive, a corresponding improvement in the tumor response would be observed if this interpretation is correct.⁴

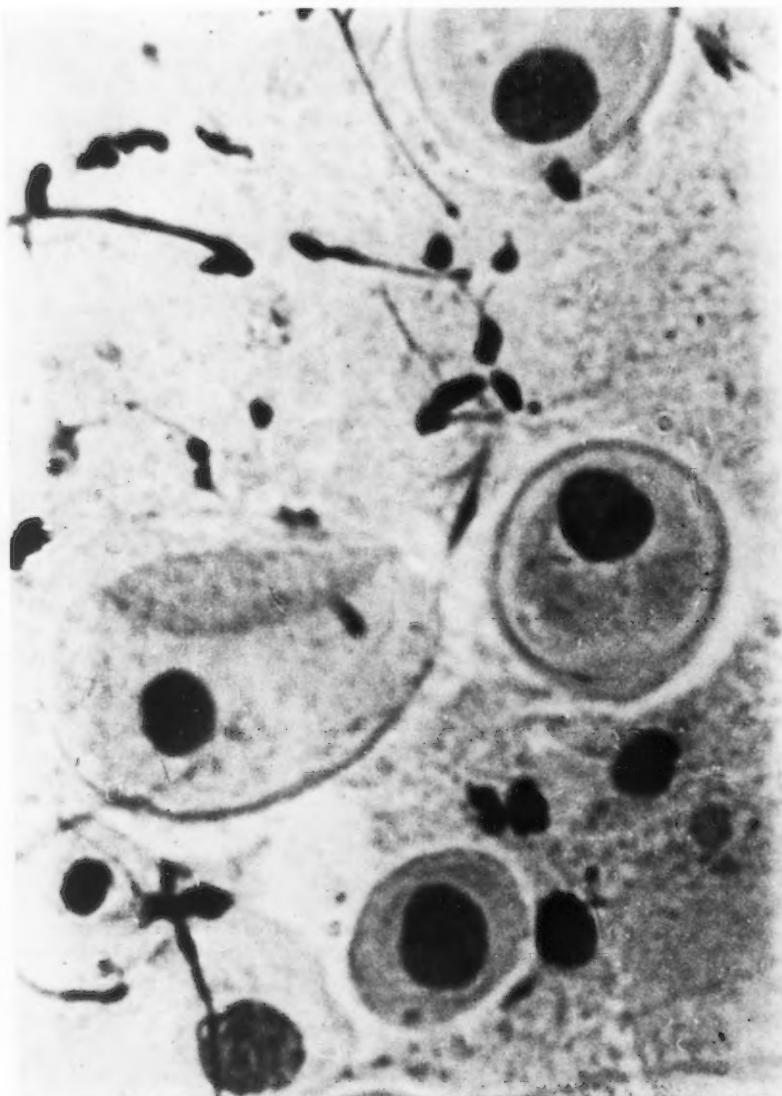


FIGURE 1. Normal basal cells. ($\times 1900$.)

How may one alter the sensitivity of an individual to irradiation? Actually, there are a number of agents that apparently

have this effect.¹ Two that have been used are: testosterone propionate given intramuscularly, 25 to 50 mg. every other day;

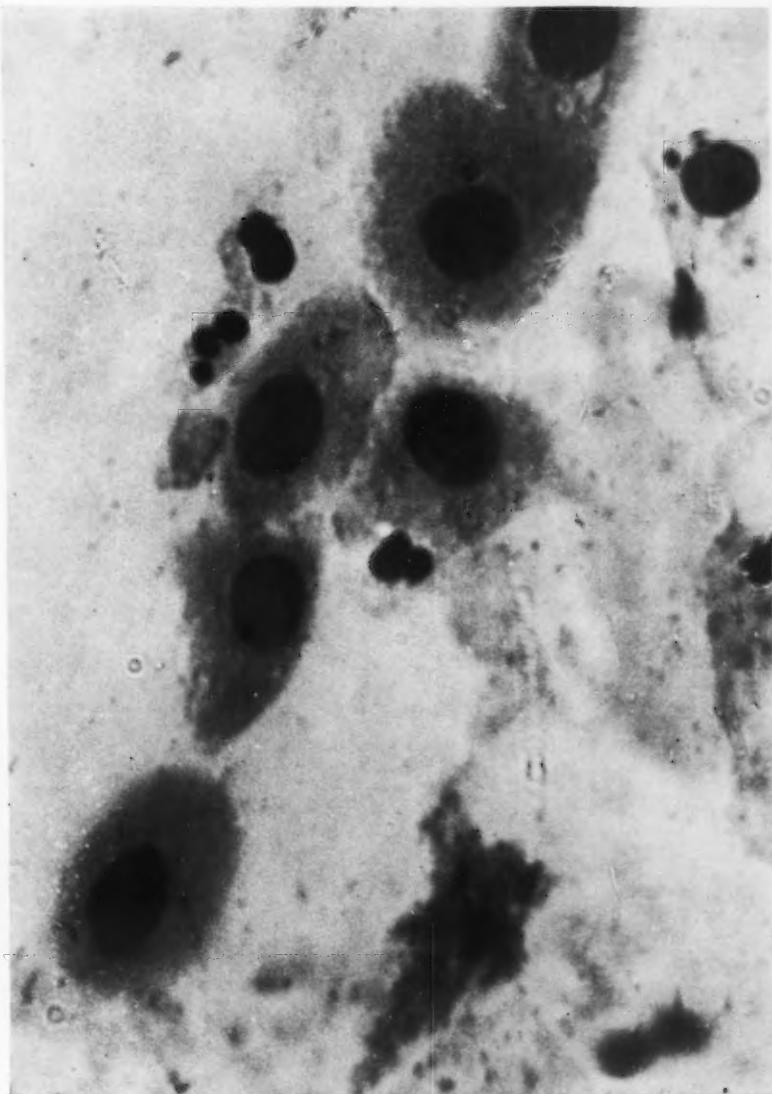


FIGURE 2. Basal cells showing SR; note the dense cytoplasm. ($\times 1900$.)

or alpha-tocopherol, 100 mg. daily by mouth. These agents were given to a series of patients who showed a poor cytological

response during the initial phase of their radiotherapy. In a pilot group of seven patients with an initially poor cytological

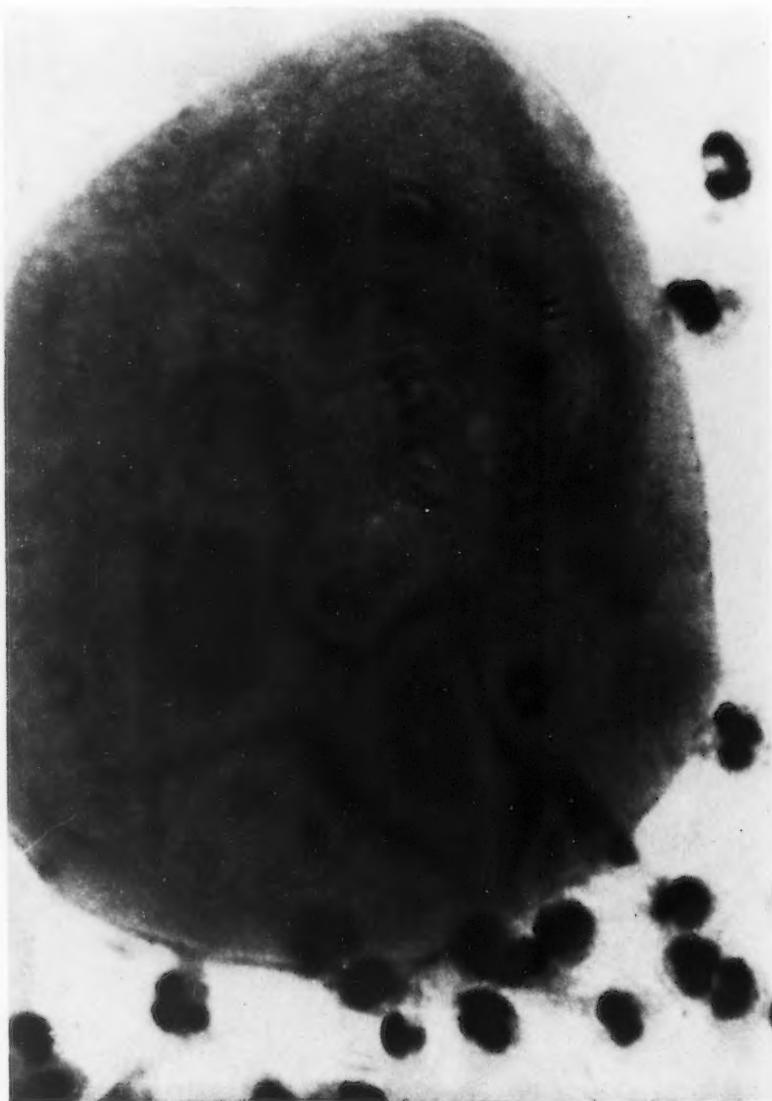


FIGURE 3. A single basal cell showing RR. Note the tremendous increase in size when compared with Fig. 1. ($\times 1900$.)

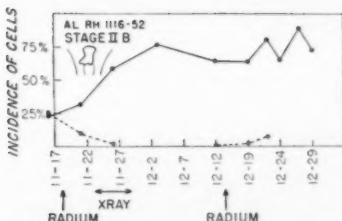


FIGURE 4. A spontaneously good cytological response. Cells showing radiation effect are indicated by the solid line and dots. The incidence of malignant cells is indicated by the broken line. The abscissa is time in days; the numbers refer to the month and day.

response treated in this manner, six attained a level of 75 per cent or more cells showing radiation effect. Accordingly, a larger series was studied at the Radiumhemmet in Stockholm, through the hospitable collaboration of Dr. H. L. Kottmeier, chief of the Gynecologic Division. Of ninety-nine consecutive cases treated radiologically, thirty-nine were found to have a spontaneously good cytological response, and sixty had an initially poor cytological response. Of the latter group, fifty-one received supplemental medication (tocopherol or testosterone) during the remainder of their radiotherapy, and, of these, thirty-three ultimately attained

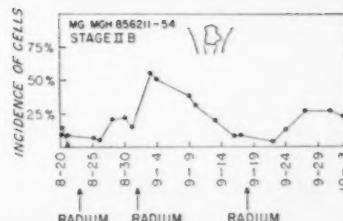


FIGURE 5. A poor cytological response.

a "good" level of RR, thirteen failed to reach 75 per cent cells showing radiation effect, and five could not be evaluated because the slides were broken before study could be completed. Nine patients with a poor cytological response received no supplemental medication, owing to language difficulties.

In Table 5 the distribution of these cases and their course in the first year is indicated. Obviously the results of treatment cannot be evaluated in one year, but the trend is suggestive and the entire mortality rate of 12 per cent is about one half of that expected.

However, this series does establish that a poor cytological response may be changed to good in almost three quarters of the cases given supplemental medication. Only time will tell whether the su-

TABLE 5
**Cancer of the Cervix Treated Radiologically at the Radiumhemmet,
Stockholm, 1952-1953—One-Year Results**

Cytological response	No.	Dead	Recurr.	Symptom free No.	%
Spontaneously good	39	2	4	33	85
Poor.* Changed to good	33	4	4	25	76
Poor.† Treated; unchanged	13	4	1	8	62
Poor.‡ Untreated	9	2	4	3	33
Poor.§ Treated; ?changed	5	0	0	5	
TOTAL	99	12	13	74	

*Initially poor cytological response. The patients were given supplementary medication: testosterone propionate, intramuscularly, 25 mg. three times a week, or α -tocopherol, 100 mg. p.o., daily, during the remainder of radiotherapy.

†Initially poor cytological response. Supplementary medication given, but the cells showing radiation effect never reached 75 per cent.

‡A poor cytological response. No supplementary medication given.

§Initially poor cytological response. Supplementary medication given. The final cytological response was undetermined owing to loss of the slides.

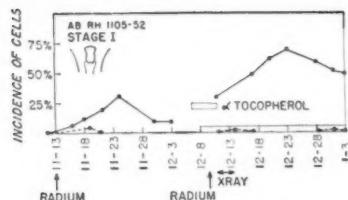


FIGURE 6. An initially poor cytological response treated with α -tocopherol, 100 mg. daily as indicated. A maximum level of 75 per cent cells showing radiation effect was attained on December 23.

perior cytological results will be paralleled by comparable improvement in the clinical course, but the initial results are encouraging.

In this period of rapid advance in the physical aspects of radiotherapy (multi-million volt roentgen rays, isotopes, etc.) it is well to recall that biological factors are of equal or greater importance. Attention to the general condition of the patient, correction of her anemia, replenishment of her nutritional reserves, gentle eradication of infection, and provision of rest during radiotherapy and its convalescence will vastly improve the effectiveness of treatment. In the past, radiation was given all too frequently on an outpatient basis, while the patient continued to keep house, and with no attention to the details just mentioned. Numerous clinics have demonstrated that the results of radiotherapy are materially improved by the same careful preparation, maintenance, and convalescence accorded a patient facing the most major surgery. Mc-Kelvey, whose five-year cure rate of 54 per cent in 256 cases is equivalent to the

best anywhere, ascribes his superior results to the hospitalization and general care the patients received in addition to their careful irradiation.

The application of all of these principles results in a program as follows:

Preliminary hospitalization is provided for study and preparation of the patient.

Stage-I and early stage-II patients with poor SR are treated with radical hysterectomy and regional lymphadenectomy.

All cases with marked SR are given primary radiotherapy.

Advanced stage II, III, and IV with poor SR are given radiotherapy and supplemental testosterone propionate or alpha-tocopherol.

All cases receiving radiotherapy are followed by means of vaginal smears. Those who fail to attain a favorable cytological response are re-evaluated with a view to immediate surgical intervention.

Summary and Conclusion

The type of treatment that will be most effective in early carcinoma of the cervix can be determined from the vaginal smear prior to treatment. Observation of the vaginal smear during radiotherapy will distinguish additional patients in whom the treatment is ineffective. The effectiveness of radiotherapy may be enhanced by attention to the general condition of the patient and by the administration of supplemental agents such as testosterone propionate or alpha-tocopherol.

Application of these principles may reasonably be expected materially to improve the salvage rate in cancer of the cervix.

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Exfoliative Cytology in Mass Screening for Uterine Cancer

Memphis and Shelby County, Tennessee

Cyrus C. Erickson, M.D.

About three years ago, a co-operative project was begun for screening the female population more than 20 years of age for uterine cancer by means of the vaginal-smear test. Approximately one half of this population of 165,000 women has now been screened. One half of these were private patients of physicians in Memphis and Shelby County and the other half were from clinics, health centers, hospitals, and annual industrial clinics.

Positive or suspicious smears were found in 1.9 per cent of the first 70,000 women screened. Biopsies were completed in 81 per cent (1077) of these cases. Biopsy showed 544 (0.78 per cent

of 70,000) cancers of the uterus—invasive and intraepithelial. Two hundred eighty-two (0.4 per cent of 70,000) were intraepithelial or noninvasive. Fifteen per cent of the 1077 biopsies showed atypical or inconclusive lesions. Suspicious smears from 293 cases gave negative biopsies, constituting 27 per cent of the biopsy group. False-positive and false-negative reports in this series were less than 0.1 per cent. It is interesting to note that 60 per cent of the 544 invasive and non-invasive cancers found were previously unsuspected—no signs or symptoms—and that this unsuspected group included many of the invasive cancers.

The intensive efforts toward education of the public by the American Cancer Society, Inc., the National Cancer Institute, and many other health organizations

From the Institute of Pathology, University of Tennessee, Memphis, Tennessee.



The Cytology Laboratory, University of Tennessee

contributed to the success of the project. Fifty-five Memphis industries employing fifty or more women co-operated in this study. Clinics were arranged for a single day or several days. City and county schools were utilized for these detection clinics. Clinics were held in six Memphis housing projects.

Repeated screening at yearly intervals is planned. After a few years, such a study should yield important facts concerning uterine cancer.

Conclusions

1. Exfoliative-cytology technique in mass screening for detection of uterine cancer is an efficient, practical test.
2. Detection by this method must be co-ordinated with the essential follow-up investigation by pathological studies of tissue biopsies for early diagnosis.
3. The greatest hope for increasing the five-year-survival rates lies in detection while the lesion is confined to the cervix.

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Current Books of Interest

ADVANCES IN CANCER RESEARCH, Vol. II. Edited by JESSE P. GREENSTEIN, PH.D., National Cancer Institute, U. S. Public Health Service, Bethesda, Maryland, and ALEXANDER HADDOW, M.D., Chester Beatty Research Institute, Royal Cancer Hospital, London, England. New York. Academic Press Inc. 1954. 530 pages with numerous graphs and tables. \$11.00.

CANCER: DIAGNOSIS, TREATMENT, PROGNOSIS, 2d ed. By LAUREN V. ACKERMAN, M.D., Professor of Surgical Pathology and Pathology, Washington University School of Medicine, St. Louis, Missouri, and JUAN A. DEL REGATO, M.D., Director Penrose Cancer Hospital, Colorado Springs, Colorado. St. Louis. C. V. Mosby Co. 1954. 1201 pages with 725 illustrations. \$22.50.

CANCER: RACE AND GEOGRAPHY. SOME ETIOLOGICAL, ENVIRONMENTAL, ETHNOLOGICAL, EPIDEMIOLOGICAL, AND STATISTICAL ASPECTS IN CAUCASOIDS, MONGOLOID, NEGROIDS, AND MEXICANS. By PAUL E. STEINER, PH.D., M.D., Professor of Pathology, University of Chicago, Chicago, Illinois. Baltimore. Williams & Wilkins Company. 1954. 363 pages with 73 illustrations. \$5.00.

THE PHYSIOPATHOLOGY OF CANCER. Edited by F. HOMBURGER, M.D., Research Professor of Medicine, and W. H. FISHMAN, PH.D., Research Professor of Biochemistry, Tufts College Medical School, Boston, Massachusetts. New York. Paul B. Hoeber, Inc., 1953. 1031 pages. Illustrated. \$18.00.



Clinicopathological Conference, Free Hospital for Women, Brookline, Massachusetts

Synthesized by Arthur T. Hertig, M.D., and Hazel Mansell, M.B., B.S.

The following case has been presented at Clinicopathological Conferences at the Free Hospital for Women on three occasions—once each in 1952, 1953, and 1954. Various members of the senior clinical staff including Dr. George Smith, Dr. Paul A. Younge and Dr. Joseph H. Phillips, together with the pathologists Dr. Arthur T. Hertig and Dr. Hazel Mansell, have taken part in the discussion. No verbatim record of these clinicopathological conferences is available and therefore the case is here presented as a composite dialogue between clinician and pathologist.

History

Mrs. L. W. (FWH Unit no. 22,793) was first seen at the age of 43 in May, 1944, with a chief complaint of profuse menstrual flow for years. This had gradually been getting worse. Although occurring every twenty-eight days, her periods lasted eight to nine days, were very profuse with large clots for four days, and were accompanied by backache. She had three children, the last delivery being in 1930. She had had no abortions. There was neither discharge nor intermenstrual bleeding. Systems review was essentially negative.

On physical examination, the blood pressure was 130/90 mm. of mercury. The patient was very obese. The uterus was somewhat large and symmetrical with cervix and pelvis negative except for lacerations of perineum and cervix. She was admitted to hospital in May, 1944, a

dilatation and curettage done, and 2400 mg.-hr. of radium given. The uterine cavity was smooth and there was a large amount of curettings. Diagnosis (S-44-1278) was "proliferative endometrium with mild hyperplasia."

She bled small amounts for short periods of time, off and on, following her radiation. At various times throughout the period she was on small quantities of estrogenic hormone, as she complained of hot flushes. A diagnosis of diabetes mellitus had been made in 1951, apparently because of transient glycosuria, for this was not later clinically substantiated.

At the age of 51 she was seen by a second doctor on April 30, 1952, because she had noted vaginal staining on two occasions three and two months before and had a history of having flowed once or twice a month for at least a year prior to that. She also complained of pain in the pelvis on coughing and a feeling of something dropping out. Her blood pressure was 220/110 mm. of mercury; her weight, 209½ lb. On examination, the uterus was slightly enlarged and pushing the uterus upward caused pain. There was a moderate-sized cystocele and a ½-in. cyst on the anterior vaginal wall. The cervix was enlarged but the Schiller test, negative. The Papanicolaou smear was class II (atypical benign). She was given buccal Oretone, 5 mg. per day for a month. One month later she reported fairly profuse bleeding on one occasion but stated that Oretone made her "feel wonderful." An operation was recommended but was postponed by the patient for personal rea-

sions until July 8, 1952, approximately eight years after first being seen with the complaint of menorrhagia.

CLINICIAN: The significant features in the history of this case as I see them are: An obese patient with a long history of premenopausal menorrhagia owing pathologically to mildly hyperplastic endometrium and treated by the administration of 2400 mg.-hr. of intracavitary radiation. Following the latter, while still on stilbestrol for menopausal symptoms, she bled on numerous occasions until she came to operation (I presume hysterectomy) eight years after seeking medical aid.

PATHOLOGIST: Why is obesity an important factor in this case?

CLINICIAN: Because obesity and other endocrine disorders, including diabetes mellitus, together with a history of dysfunctional premenopausal bleeding owing to hyperplastic endometrium, are significantly more common in patients who ultimately develop endometrial carcinoma.

PATHOLOGIST: If you think this patient was "threatened" with the development of endometrial carcinoma, why do you suppose the patient's physician treated her histologically benign but clinically "precarious" endometrial lesion by a non-cancericidal dose of radium amounting to only 2400 mg.-hr.?

CLINICIAN: At that time (1944) this was considered an excellent method for the artificial induction of the menopause in patients who had dysfunctional bleeding owing to benign endometrial lesions, especially in poor operative risks. This patient, you will recall, was very obese. It is only relatively recently, through the work of Corscaden and his co-workers at Columbia's Presbyterian Hospital as well as of other workers, that we have come to realize the potential danger in the radiation-induced menopause, since the patients seem to have three to four times the expected incidence of endometrial cancer.

PATHOLOGIST: By danger, do you mean that the radiation induces the histologically benign endometrium to undergo malignant change?

CLINICIAN: No. There is no proof that

radiation induces such changes, although there is significant increase in the number of carcinosarcomas following such therapy, suggesting that the radiation had some neoplasm-inducing effect on the endometrial stroma. Even though there is no proof that radiation per se induces endometrial cancer (although it does so in other organs such as the skin and bone marrow), we must remember that these irradiated patients with benign bleeding are the very ones who, statistically, are more apt to develop endometrial carcinoma than their sisters who do NOT have premenopausal dysfunctional bleeding. Moreover, the fact that a patient has been irradiated seems to give her and her physician a false sense of security, especially if no more uterine bleeding occurs.

PATHOLOGIST: But this patient did have additional bleeding off and on after her radium-induced menopause. Why do you suppose that her physician failed to take more definitive steps in treating this bleeding?

CLINICIAN: Probably because the patient was on stilbestrol and therefore the slight irregular bleeding was no doubt interpreted as being withdrawal type because of "teetering" in the level of the estrogenic hormone.

PARTHOLIST: Assuming, for the sake of discussion, that the bleeding between the 1944 dilatation and curettage with radium insertion and the operation in 1952 was not due to the therapeutically administered stilbestrol, what are the possible causes of scant and irregular, though persisting, bleeding?

CLINICIAN: There are two groups of causes: (1) local, such as inflammation, endometrial hyperplasia, polyp or polyps, or a cancer (possibly present in 1944, but in one cornu or behind a fibroid and so unavailable to the curette); and (2) ovarian (with secondary effect on the endometrium), such as cystic follicles, cortical-stromal hyperplasia, or a feminizing mesenchymal tumor, such as a thecoma, a granulosa-cell tumor, or the rare variant, the luteoma.

PARTHOLIST: Would not the radiation have caused the suppression of hormone

production by any of the ovarian tumors that you have mentioned?

CLINICIAN: No. Ionizing radiation affects only the primordial ova and not the component parts of the follicle wall or the hyperplastic or neoplastic derivatives thereof.

PATHOLOGIST: Could the radiation have induced any of the ovarian lesions following the death of the primordial ova?

CLINICIAN: It is possible although not probable. You will recall the case in this hospital of the 38-year-old patient who developed a granulosa-cell tumor after four exposures to roentgen rays, received while being allowed to sit beside her mother during therapy for breast cancer. In general, however, patients with cancer of the cervix treated primarily by radiation have no appreciably increased incidence of feminizing mesenchymal tumors, even though such tumors may be induced in mice by small doses of roentgen rays.

PATHOLOGIST: For the final question, before the surgical pathology underlying this case is stated, what do you think is the most likely cause of bleeding in this patient?

CLINICIAN: An endometrial polyp, probably benign. There is no way in which the clinical data given would rule in or out a previously undetected endometrial carcinoma. Although the uterus is slightly enlarged the patient is obese and therefore pelvic examination was unsatisfactory. A small submucous fibroid could have caused her persistent bleeding.

PATHOLOGIST: From the data given, can you rule an ovarian lesion in or out?

CLINICIAN: No. Perhaps her clinician could give us the details of his preoperative examination done under anesthesia. What was the preoperative diagnosis?

DR. PAUL A. YOUNG: Examination under anesthesia revealed a moderate-sized cystocele. There was a lacerated, well-healed cervix, and the fundus of the uterus was slightly enlarged. Behind the uterus on the left side was a firm mass suggesting a pedunculated fibroid or ovarian cyst, measuring about 6 cm. in diameter. This was not felt prior to this examination probably because of the patient's obesity.

An exploratory laparotomy was done in order to ascertain the nature of this mass and on the clinical grounds of postmenopausal bleeding. The essential preoperative diagnosis had been postmenopausal bleeding, with a definitive cause not being known but the possibility of cystic ovaries being considered. On July 8, 1952, a routine anterior colporrhaphy was done and then, at laparotomy, the fundus of the uterus was found to be enlarged; the left ovary was replaced by a multilocular cyst, blue in color; and the right ovary was about three times normal size with a firm cystic structure at each pole, measuring 1.5 to 2.0 cm. in diameter. Complete hysterectomy with bilateral salpingo-oophorectomy was done.

PATHOLOGICAL diagnoses were as follows (S-52-2822):

Chronic cervicitis with adenomatous hyperplasia

Cystic and polypoid hyperplasia of the endometrium with adenomatous hyperplasia and carcinoma in situ

Adenomyosis uteri and leiomyoma uteri (intramural)

Tubes negative for disease

Granulosa-cell carcinoma of the ovary, bilateral

Peritoneal inclusion cysts

Portion of vagina that was essentially negative

PATHOLOGIST: This case is of interest for several reasons:

1. It illustrates that, although often successful, radiation induction of the menopause may occasionally fail because of the presence of local endometrial or general ovarian lesions that are not suppressed by the small amounts of radiation given (2400 mg.-hr.). This case illustrates very well Corscaden's concept that, although radiation probably does not induce endometrial cancer, the latter is more apt to develop in those patients because of the lesions for which the patient was irradiated. Stated differently, this is an example of the false sense of security engendered in both patient and physician after irradiation for benign endometrial bleeding.

2. Polyps and endometrial hyperplasia

are "precancerous" in the broad sense, although only a small fraction of such lesions become malignant. Corscaden's figures show that patients with premenopausal hyperplasia of the endometrium treated by a radiation-induced menopause are ten times as apt to develop endometrial carcinoma as similarly treated patients who do not have hyperplasia. Stated somewhat differently, about 1.5 per cent of endometrial hyperplasias in patients with a radiation-induced menopause are followed by endometrial carcinoma.

3. So-called "active" feminizing mesenchymal tumors, of which these granulosa-cell carcinomas were examples, are twice as apt to provoke active lesions in the endometrium as are "inactive" tumors. ("Activity" in such tumors as thecomas, granulosa-cell tumors, and luteomas includes the presence of mitoses and of plump or fusiform theca cells, with or without luteinization but with absence of extensive collagen deposition, and the presence of K-cells, histochemically shown to contain ketosteroids, presumably hormones. These K-cells are comparable to those shown in the normal graafian follicle and corpus luteum.) Of interest in this case is the fact that "active" feminizing mesenchymal tumors are more than three times as apt to have an associated endometrial carcinoma *in situ* or actual carcinoma than are the "inactive" ovarian tumors of this type. Many authors have noted the correlation between the presence of feminizing mesenchymal tumors and endometrial carcinoma. At the Free Hospital for Women, of eighty cases of feminizing mesenchymal tumors reviewed by Mansell and Hertig, eleven, or 15 per cent, had endometrial carcinoma and another 9 per cent had carcinoma *in situ*. If one considers only patients more than 50 years of age, the incidence of endometrial carcinoma in our cases and in those reported in the literature is approximately 25 per cent. This is to be expected in view of the average of 55 years for patients with endometrial carcinoma.

4. Granulosa-cell tumors are all potentially malignant but, when they are morphologically malignant, as the tumors

were in this patient, the prognosis is poor and the clinical course rapidly fatal, two years and five months after diagnosis in this case.

Postoperatively the patient did well and concluded her roentgen-ray therapy within three weeks. A month later, however, she had a cholecystectomy and exploration of the common bile duct for cholecystitis and cholelithiasis. Eight months postoperatively the patient was reoperated upon for the repair of an enterocele. At this time anterior colporrhaphy and perineorrhaphy were done. There was no evidence of recurrence (or persistence) of the granulosa-cell carcinoma until about eighteen months postoperatively, when there was evidence of pleural and ascitic fluid. On tapping, this contained malignant cells consistent with an origin from granulosa-cell carcinoma (S53-5624). During the next year the clinical course was progressively downhill, complicated by the reaccumulation of chest and abdominal fluid. This required tapping every two or three months. An additional 2400 r of roentgen rays was given (1200 to chest and 1200 to abdomen) two years postoperatively and six months prior to death.

Death occurred of generalized carcinomatosis (no autopsy performed) approximately two and a half years after the hysterectomy and bilateral salpingo-oophorectomy—ten and a half years after the radium-induced menopause for dysfunctional bleeding caused by endometrial hyperplasia. The latter may or may not have been the result of estrogen stimulation from bilateral granulosa-cell tumors, since it is not known under what conditions they arise. In any event they were present two and a half years before and were responsible for the patient's death.

In summary, this patient epitomizes the potential danger of endometrial carcinoma in a radiation-induced menopause and its relationship with estrogen-producing lesions of the ovary and their role in the pathogenesis of endometrial carcinoma. The cause of death was generalized carcinomatosis resulting from bilateral granulosa-cell tumors.



DOCTORS' DILEMMAS

Q Clinically and according to the roentgenologist, my patient, a man aged 47, has carcinoma of the stomach. In preoperative work-up, the patient, who is not jaundiced, was found to have an alkaline phosphatase of 11.2 Bodansky units. Does this finding suggest spread of his cancer to the liver?

A It is extremely likely that this patient does have metastases to the liver providing there is no evidence of a primary liver disorder demonstrated by other liver-function tests. In the absence of jaundice, elevated alkaline phosphatase is seen in patients who have Paget's disease of bone or other osteoblastic processes involving bone. If these are excluded, there is great likelihood that the patient has liver metastases.

Q A 44-year-old woman, gravida III, para III, had a pelvic laparotomy in 1947, with an abdominal supracervical hysterectomy and bilateral partial oophorectomy for metrorrhagia and vaginal discharge owing to uterine fibroids. Prior to her hysterectomy she had had menorrhagia for a long time. Her deliveries were in 1931, 1933, and 1936. Menses had always been regular. There had never been any masses in the breasts or cysts that formed in the breasts with her periods.

For the past ten years (since 1944), she has had a serous, clear drainage from her right nipple. This drainage was at first intermittent but, for the past three years,

has been continuously present daily. In addition, she has had bleeding from this nipple for a period of about one week, intermittently, for the past four years. The bleeding is rather heavy. There is no visible lesion or incrustation on the nipple skin. There is no tumor palpable in the axillae or in either breast. No retraction or change in the skin of the breast is visible. A Papanicolaou smear of the serous discharge was reported negative for malignant cells.

Her family physician, also a personal friend, advised her to leave the breast alone, as long as there is no change for the worse.

Realizing that this may be a low-grade carcinoma or intraductal papilloma that has already existed over a period of years, I too am reluctant to advise an exploration of the breast, since this is tantamount to suggesting a simple mastectomy in this case. What would be sound advice for this patient?

A It would be wise to have several careful repeat examinations of smears of the nipple secretion. Another thing that should be done is to identify, if possible, the duct from which the blood appears to be issuing. If this duct can be identified, a needle may be inserted in it and, by injecting a suitable radiopaque substance, a partial mammogram may be obtained, which will sometimes disclose an intraductal tumor that is not palpable. It would seem that the best management of this patient is an exploration of the duct system suggested

by the orifice from which the blood is appearing. This does not necessarily involve a mastectomy but simply an excision of the segment of the breast, usually limited to the subareolar portion, in which the duct pathology is encountered.

Q Two months ago I saw a patient with a hemoglobin of 7 gm. Complete hematological studies, including bone-marrow aspiration, were normal. A complete gastrointestinal survey was unremarkable. The patient was transfused and immediately was asymptomatic. Two weeks later his hemoglobin had fallen from 15 to 10 gm. During the last three weeks, on a meat-free diet, he has been found to have persistent occult blood in stool specimens.

A repeat gastrointestinal series and barium enema are again unremarkable. Hematological studies reveal no condition to account for the bleeding. Am I justified in insisting on an exploratory laparotomy for this patient?

A Yes. This should certainly be done, since a small lesion of the gastrointestinal tract may escape the most competent radiologist. Occult blood in the stool is a certain sign of bleeding from the gastrointestinal tract. Lesions most likely to be found are polyps, tumors of the small intestine, small ulcerating carcinomas of the stomach, lipomas involving the gastrointestinal tract, leiomyosarcomas, or the more rare Meckel's diverticulum or chronic intussusception.

References to Neoplasms of the Uterus in Previous Issues of CA

1:84, March, 1951 Classification of cervical cancer.

2:50, March, 1952 Present status and future trends of exfoliative cytology.

2:57, March, 1952 Cytological techniques in screening uterine and lung cancer.

2:63, March, 1952 The gynecologist views cytology—past, present, and future.

3:184, Sept., 1953 Office experience with the cytological technique.

3:188, Sept., 1953 The diagnosis of early carcinoma.

3:205, Nov., 1953 Periodic examination of the female pelvic organs and breasts; report of a fifteen-year research on the control of cancer.

3:208, Nov., 1953 Radiation versus surgery in the treatment of cancer of the cervix.

3:212, Nov., 1953 Exfoliative cytology as a case-finding procedure for general-population screening.

3:218, Nov., 1953 Management of cervical cancer complicated by pregnancy.

4:155, Sept., 1954 The differential diagnosis of benign and malignant pelvic lesions in women.



new developments in cancer

Indicted as Pathogens . . .

W. C. Hueper (National Cancer Institute), discussing occupational and industrial causes of disease, lists as disease-causing agents to which the population more and more is exposed: pesticides, herbicides, defoliants, growth promoters, vehicles of sprays, solvents, dry-cleaning agents, detergents, waxes, polishes, plastics, resins, preservatives, food additives, paints, dyes, medicines, cosmetics, fuels, lubricants, industrial wastes, gasoline- and diesel-engine exhausts, and dust from asphalt and oiled roads and rubber tires. Hueper states that symptomatically and pathologically, occupational and industrial ailments, especially in their chronic forms, often mimic diseases of infectious, hormonal, or metabolic origin; and he urges that complaints be interpreted with some regard for occupational exposures. He asserts that almost all organs and tissues may be involved and lists as the possible consequences of exposure: neurotoxicoses and psychoses, toxic and allergic dermatitis and skin cancers, chemical pneumonitis and pneumoconioses, arthritis, osteoporosis and osteosclerosis, anemia, agranulocytosis, erythrocytosis and leukemia, hemorrhagic diathesis, toxic and allergic arteritis, arteriosclerosis and

atherosclerosis, nephrosclerosis and nephrosis, hepatitis and acute yellow atrophy, gastric ulcers, colitis, gynecomastia, and testicular atrophy.

Liver Cancer in Hong Kong . . .

Hou Pao-Chang (Honk Kong), basing his conclusions on 150 cases of primary liver cancer studied at necropsy, has reported an association between that disease and infestation by *Clonorchis sinensis*. He asserts that in a number of cases the cancer arose from infestation of the adenomatoid tissue of the bile ducts.

Dog's Life . . .

Dogs sick with cancer have been a testing ground for a series of new ethyleneimines produced by Dr. Moses L. Crossley of Rutgers University. The animal tests helped establish dosages for humans and indicated which compounds held the most promise. Dr. John R. McCoy, veterinarian and pathologist, who conducted the tests, said the eighty animals treated over the last three years (at a cost of about \$450 a dog) were much more satisfactory for chemotherapeutic trials than rats, mice, or other more conventional laboratory animals. The drugs appeared to

add to the dogs' life spans, and they seemed to afford subjective and objective improvement for as long as thirty months. The more beneficial ethyleneimines were TEPA, thio-TEPA, MEPA, and ODEPA.

Is Cancer a Mutation? . . .

Dr. Walter J. Burdette (Louisiana State University) cautioned the VI. International Cancer Congress against "succumbing to the tempting assumption that the change to malignancy is necessarily a somatic mutation." He said that mutation is a questionable explanation of cancer.

His doubt springs from these observations: (1) methylcholanthrene increases the tumor rate in fruit flies but not the number of germinal mutations; (2) methylcholanthrene induces tumors in JK mice, but it does not increase the mutation rate; (3) a mutation gene (which causes other genes to mutate) did not raise the cancer frequency when introduced into the chromosomes of two fruit-fly strains; and (4) 1,2,5,6-dibenzanthracene and methylcholanthrene did not step up fruit-fly-mutation rates.

Cancer of the Hypopharynx . . .

The surgeons seem to have won a round over the radiotherapists at the VI International Cancer Research Congress in São Paulo, Brazil, on treatment for cancer of the hypopharynx. World radiation cure rates for this condition range from 3 to 16 per cent. Dr. H. Mason Morfit (University of Colorado) reported that five of sixteen such cases are alive and apparently well three years after radical surgery. There were no surgical deaths. A larger series at Memorial Center for Cancer and Allied Diseases, New York, shows about the same survival rate, since that hospital's shift from radiation to surgery for cancer of the hypopharynx.

The success of good radiotherapists in treating cancer of the larynx, on the other hand, has some surgeons saying they would try radiation first for this condition.

Hepatotoxins . . .

Liver-damaging substances encountered in various occupations include halogenated hydrocarbons, aromatic and cyclic hydrocarbons, some alcohols, ether, glycol derivatives, and nitro compounds reports J. Robert Teabeaut II (Washington). He cites as metals giving rise to toxic hepatitis: manganese, arsenic, phosphorus, tellurium, plutonium, and thorium. Exogenous toxic hepatitis is characterized by: (1) necrosis of liver cells, usually in zonal pattern, (2) absence of inflammatory reaction, (3) fatty degeneration of hepatic cells, and (4) preservation of reticular fibers.

Calcium:Magnesium Ratio in Cancer . . .

Dr. Albert Striebel (Basle) proposes the urinary Ca:Mg ratio as a diagnostic aid in cancer. Dividing these ratios, which vary from 0.1 to 7.8, into three types: (1) less than 0.8, (2) between 0.8 and 1.2, and (3) more than 1.2, he finds 21 per cent of normal persons in type 1, 50 per cent in type 2, and 29 per cent in type 3. In noncancerous, hospital patients these figures were 39, 31, and 30, and in cancerous patients 42, 8, and 50. In the presence of osteolytic lesions, calcium values (and the Ca:Mg ratio) are higher than normal; and, in the absence of osteolytic lesions with anorexia and wasting of soft body tissues, calcium values (and the Ca:Mg ratio) are lower than normal. Ratios less than 0.8 and greater than 1.2 are statistically suggestive of cancer. Further study is required for full evaluation of these Ca:Mg ratios.

Glücksmann (Strangeways Lab., England) reported somewhat similar observations. His therapy decisions are based largely on radiation's forcing the cancer cells to differentiate. (He states that radiation either kills cancer cells or makes them differentiate.) He is investigating the effect of the host upon the tumor in the belief that the former can be altered to affect the latter. Sex hormones and vitamin E sometimes change the host's response. Glücksmann, like the Grahams, is testing the theory that patients nonresponsive to radiation are good candidates for surgery and vice versa.

Cuyler (Duke U.) concluded from a study of 155,000 smears from 43,000 patients that essentially normal genital cytology is found in only one in six to eight patients.

Brack (Johns Hopkins U.) said that 262 cervical cancers were detected in a series of 4598 smears and biopsies on 2180 patients. The first biopsy was correct in 97.4 per cent of the cases, the first smear correct or doubtful in 87.4 per cent. He cautioned against treatment without biopsy confirmation of positive cytology. Cure rates for carcinoma *in situ* run about 100 per cent and for stage I 75 per cent, and for this reason he takes no chances in allowing stage 0 to become stage I.

Way (Newcastle-upon-Tyne, England) asserted that radiation and surgery often cure the same type of tumor, leaving a great number that cannot be cured by either method. He believes that nutrition may play some part in curability. Many English women "starved for protein for about twenty-five years" (during depression, war, and postwar austerity) do not respond well to radiation treatment for cervical cancer. Among these, cure rates are substantially lower than in better-fed populations.

Scheffey (Jefferson Medical College) urged biopsy for women more than 40 years of age who complained of irregular uterine bleeding. He said that the widespread and indiscriminate use of hormone therapy for irregular bleeding in this age group and for the relief of "menopausal symptoms" should be discontinued.

Homburger and Kasdon (Tufts) asserted that beta-glucuronidase activity in vaginal fluid can be measured with great accuracy and that it is elevated in 80 per cent of premenopausal women with invasive cervical carcinoma. Fishman has said that an elevation frequency indicates not only cancer but precancerous infections that are readily

cleared upon discovery. The Tufts group feel that, as a mass screening test, this may call attention to most young patients with cervical cancer when the disease is in its most curable state and practically eliminate it as a significant cause of death among young women.

Treatment: Surgeons and radiotherapists squared off under a caution from Moderator Cameron (ACS) that in discussing treatment of cervical cancer, the question is not who is right, but what is right for the patient.

Taylor (Columbia-Presbyterian) cited five schools of thought on the scope of surgery: (1) only stage-I and -II cases unresponsive to radiation; (2) all stage-I cases; (3) all stage-I and -II; (4) practically all cases in which there are no strong medical contraindications; and (5) assorted other situations including surgery only for those which radiation cannot cure in the first place.

Meigs (Mass. Gen. Hosp.) described the Grahams' radiosensitivity tests as a practical objective criterion for radiation or surgery.

Brunschwig (Memorial Center) traced the re-emergence of surgery in the field of cervical-cancer treatment and described as one of its roles the salvage of cases after radiation has failed, as well as that of affording a high rate of cure in early cases. He said that, on the other hand, radiation frequently does little for those whom surgery cannot save.

del Regato (Penrose Cancer Hospital) declared that adequate radiation today can save between 40 and 50 per cent of all patients, but he emphasized that fine equipment is no substitute for medical skill. In 222 unselected cases (one half, stages I and II; the other half, III and IV), 37 per cent of all cases and 28 per cent of the stage-III and -IV cases remain well and without signs of cancer five and ten years after treatment, he reported. His treatment consists of a high "homogeneous" dose of radiation -- roentgen rays from a source outside the pelvis and rays from radon implants inside the vagina. In this manner, all potential points of pelvic spread of the disease are irradiated. Treatment is daily for from two and a half to three months. Nine of fifty-two stage-IV cases so treated have survived five years or more and presumably are cured. (del Regato said cervical cancer recurs in only 1.5 per cent of those who are well five years after treatment, as compared with a 20 per cent loss of five-year survivors of breast-cancer operations.)

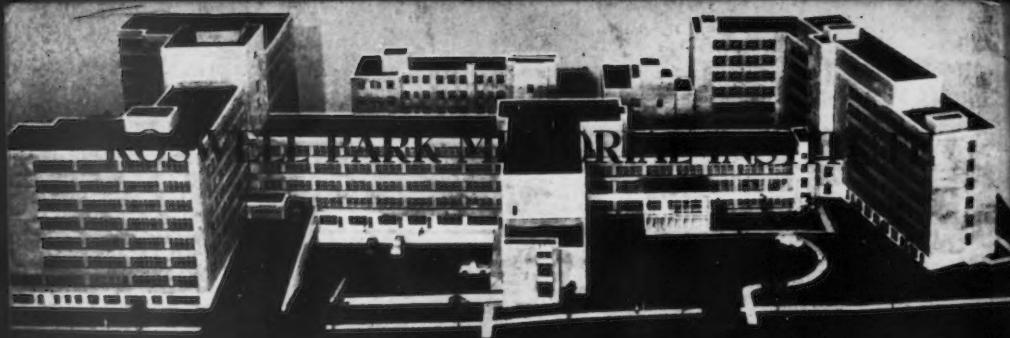
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The color photographs and text of the center spread were supplied by Paul A. Younge, M.D., Free Hospital for Women, Brookline, Massachusetts; Lewis C. Scheffey, M.D., Jefferson Medical College and Hospital, Philadelphia, Pennsylvania; and Paul F. Fletcher, M.D., St. Louis University School of Medicine, St. Louis, Missouri.

The photograph of Dr. Papanicolaou, page 53, is by Michael Hollander, *Photography*, New York City.

COMING MEDICAL MEETINGS

Date 1955	Meeting	City	Place
April 15-16	[Eighth] Annual Cancer Symposium of the James Ewing Society	New York City	Memorial Center
April 15-17	Annual Meeting, American Association for Cancer Research	San Francisco	St. Francis Hotel
April 22-23	American Geriatrics Society	New York City	
April 23-30	Industrial Medical Association	Buffalo	Memorial Auditorium
April 24-26	American Association for Thoracic Surgery	Atlantic City	Chalfonte-Haddon Hall
April 24-29	Fifth Inter-American Congress of Radiology	Washington, D. C.	Shoreham Hotel
April 25-29	American College of Physicians	Philadelphia	Convention Hall
May 1	Federation for Clinical Research	Atlantic City	
May 9-13	Medical Society, State of New York	Buffalo	Hotel Statler
May 17-19	Massachusetts Medical Society	Boston	
May 22-25	American Association of Genito-Urinary Surgeons	Monterey, Calif.	
May 23-25	American Gynecological Society	Quebec, P. Q., Canada	
June 2-4	The Endocrine Society	Atlantic City	Chalfonte-Haddon Hall
June 2-5	American Medical Women's Association	Atlantic City	
June 6-10	American Medical Association	Atlantic City	



I N S T I T U T I O N S F O R

C A N C E R R E S E A R C H

LAST October a new clinical wing was opened at the Roswell Park Memorial Institute in Buffalo. New laboratories of biochemistry and biology are to be added soon. With completion of this 12-million-dollar project, 516 beds will be available for cancer investigation.

In 1898 Dr. Roswell Park, Professor of Surgery at the University of Buffalo, on a \$10,000 State appropriation, started this institution—the first for cancer research only—in three small laboratory rooms. Now, with the addition of clinical facilities for the most modern treatment of neoplastic diseases and the installation of splendidly equipped laboratories for the paramedical sciences, the institution stands in top rank among the best equipped and staffed organizations for cancer research.

The Institute is supported largely by the State. There is no charge of any sort to the patients, who are all residents of the state and are referred by physicians licensed in the state. Patients with all types of malignant and premalignant lesions are accepted for active treatment and intensive investigation, rather than those with minor lesions that can be treated effectively elsewhere or those requiring terminal care.

In the clinical section are available all the modern diagnostic and therapeutic facilities, including two 2 million volt roentgen-ray machines, linear accelerator, and radioisotope service. Approximately 25,000 patients a year are given diagnostic and therapeutic service.

In addition to the facilities for laboratory and clinical cancer research, under-

graduate and graduate medical instruction is given by a corps of cancer specialists of the New York State Department of Health and the University of Buffalo.

Roswell Park Memorial Institute is truly a citadel of strength in the control of cancer through education and research—clinical and laboratory.

ROSWELL PARK, M.D. (1852-1914) received his medical degree from Northwestern University in 1896. After several years at Women's Medical College, Chicago, he served as Professor of Surgery at Northwestern University and Rush Medical College and then became Professor of Surgery at the University of Buffalo, where he continued until his sudden death from heart disease, February 15, 1914.

In 1898 he opened the three-room laboratory for the study of cancer—now the Roswell Park Memorial Institute.

In 1896 his *Text-Book of American Surgery* was published; in 1897, an *Epitome of the History of Medicine*; in 1907, *Principles and Practice of Modern Surgery*.

Dr. Park was an "anatomist of unusual erudition, pathologist of highest rank, surgeon of great clinical skill and rare judgment, teacher who possessed the somewhat rare faculty of making his students remember what he taught them. While a man of pronounced opinions, he was greatly beloved by his fellow practitioners, to whom he endeared himself by unfailing courtesy, and by giving without stint of his stores of knowledge." (J.A.M.A. 62: 630, Feb. 21, 1914.)

